CIRCULATORY DYNAMICS

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Physiologic Studies

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Preface

During the past year it has been my privilege to deliver several lectures on phases of circulatory physiology to which I have contributed during the past forty years Whenever necessary the original interpretations of experimental results were re evaluated in the light of subsequent work Three of these discourses dealt with experimental aspects of circulatory dynamics and it was thought that their collection in book form would prove useful to investigators and progressive practitioners interested in human circulatory dynamics The original lectures then have been reca t as chapters here

The first chapter begins with a simple exposition of hemodynamic laws analyzes the practical information which can be gained from arterial pressure readings and arterial pulse registrations and shows by way of illustration how information so gained enhances our understanding of the dynamics of hypertension

The second chapter concerns itself with the physiological mechanisms by which the ventricles adapt themselves to altered circulatory states in health and disease Theories are divorced from factual data an integration of successive new discoveries with classic laws of the heart leads to a modern concept of cardiac adaptation

The third chapter is devoted to interpretations of ventricular contraction patterns by means of critical analyses of ventricular pressure curves The discussions include alterations which take place as a result of pericardial effu ion hypervolemia oligemia arterial hypertension aortic coarctation aortic and pulmonary stenosis idioventricular rhythms ventricular alternation coronary occlusion myocardial ischemia and valvular lesions

C J W

Cleveland Ohio
April 1952

CHAPTER I

Basic Hemodynamic Principles in the Interpretation of Circulatory Disorders*

DISEASES are experiments performed by nature on animals and human beings. It is one of the responsibilities of physicians to understand the character of the human experiment going on to the end that it may be terminated or that natural compensatory mechanisms may be aided. Physicians can gain assistance in these tasks in several ways. (1) They can apply available information gained through an orderly solution of problems regardless of their apparent practical value. (2) They can be guided by information accumulated through careful clinical studies of disease. (3) They can benefit from consideration of animal experiments in which nature's disorders have been reduplicated or simulated. (4) They can by experience and continued practice improve their capacity to assess the significance of signs and symptoms. They can through the use of laboratory apparatus and technics translate phenomena which are undetectable by the unaided senses into forms which the mind can grasp. The measurement *of human blood pressures and the registration of arterial pulses are* currently giving a great deal of information in the diagnosis of circulatory disorders. But in my opinion the cardiologist in his everyday practice is still not using all the information that these procedures could yield. For this reason it appears desirable to review a number of basic principles which may enhance the value of available information.

* In substance, lectures delivered before the Washington State Heart Association, Spokane, Washington, Sept. 9, 1950 and the Postgraduate Symposium on Heart Disease, California Heart Association, San Francisco, Oct. 25, 1950.

Elementary Hemodynamics

Hemodynamics is concerned with the forces operative in the propulsion of blood around the circulatory system. The physical forces concerned have been partly derived from hydrodynamics such as are concerned in supplying water to dwellings. As illustrated in figure 1 A, water flows from a high reservoir through a series of pipes to faucets located at varying distances above ground level. The eleva

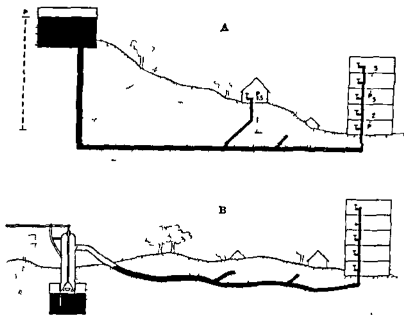


FIG 1 —Two diagrams illustrating the hydrodynamic principles determining the flow of water from faucets. A constant pressure reservoir and rigid pipe system. B rhythmic pump system through elastic hose

tion of the water surface above ground level (P) constitutes the motive force and the difference between this level and that of any faucet say P^1 is an important determinant of the greatest possible flow from the tap. If the pressure in the central reservoir rises or falls or if respective taps are located at higher or lower levels of a tall building the maximal flow from a fully opened tap will increase or decrease in proportion to the differences in elevation (or pressure) between the surface of the reservoir and the faucet

Again if two faucets (P^3) at the same elevation in a near and far dwelling are successively opened the rate of water delivery from the near one exceeds that of the far one only slightly This shows that the loss of pressure due to friction in the main delivery pipes is rather slight Of course the narrower and longer the pipe the greater the pressure drop due to resistance

Now it is a common experience that the volume of water delivered by any faucet can be regulated widely between a small drip to a full gush by the extent to which it is opened i e by the degree of friction or resistance encountered within the faucet In other words the greatest and most variable resistance is in the stopcocks Similarly the arterioles in the body represent stopcocks which by altering their caliber meter the volume of blood which enters the capillaries All of this is common sense or shall we say it borders on the moronic Expressed mathematically the rate of flow (F) varies directly with the pressure difference ($P - P_1$) and inversely with the resistance (R) mainly at the outlets of the system Such a formulation $F = \frac{P - P_1}{R}$ is the essence of Poiseuille s law with one exception viz a viscosity factor (V) It is obvious that if such a supply system were suddenly filled with a highly viscid fluid such as molasses the rate of flow from any faucet would be greatly decreased despite the fact that pressure differences and apertures of faucets (resistance) did not vary Since the viscosity of blood is approximately five times that of water and may vary under different conditions the full Poiseuille equation becomes

$$F = \frac{P - P_1}{R} \times \frac{1}{V} \text{ or transposing}$$

$$\text{Resistance } (R) = \frac{P - P_1}{F} \times \frac{1}{V}$$

Hemodynamics of Pulsating Streams While such physical principles are exceedingly useful in formulating elementary concepts of hemodynamics they describe the forces which move blood through the arterial tree and into the capillaries very incompletely This is principally due to the fact that the conduits are elastic not rigid tubes and that a pulsating not a constant pressure is created by the ventricular pump The situation could be compared to a hypothetic

water supply system such as is illustrated in figure 1 B, in which no reservoir elevation is attainable. Water can be lifted from a deep well to the surface and placed under pressure by a combination lift and pressure pump. If such water were pumped through a rigid system, water would flow out of opened faucets in a periodic fashion, accelerating with each stroke of the pump and rapidly decelerating to zero during the period that water is being lifted into the pump. If, however, the conducting system were elastic, as in the illustration, it would expand and accommodate a part of the liquid during the *stroke and recoil during the filling time of the pump, thus maintaining* a constant flow from the faucets at a higher level.

While this illustrates the mechanism of the mammalian circulation in an elementary way, precise theoretical hemodynamic deductions have proved difficult owing to the physical effects of vascular branching, the variable caliber and distensibility of muscular arteries, the reverberating pressure waves set up, the change in viscosity which takes place through filtration, osmosis, or secretion in passage of blood through capillaries. For these reasons, theoretical deductions must still be tested by experimental studies on animals.

Experimental work has established the conditions which are operative in the normal mammalian circulation. With each ventricular systole a certain volume of blood, variously called the *stroke volume*, *systolic discharge* or *pulse volume*, is expelled brusquely into the aorta. In man this equals approximately 60 or 70 cc., and the whole period of ejection lasts only 0.25 second or less. Fully two thirds of the total stroke volume (about 45 cc.) is displaced into the ascending aorta and arch within 0.1 second and very little during the last 0.05 second of ejection. Since the ascending aorta and arch are already distended under a pressure of 70 to 80 mm. Hg, it is obvious that space for some 45 cc. of blood must be made in an interval of time which would be called "instantaneous" in photography. This is accomplished partly by the forward movement of blood (*kinetic energy of flow*) and partly by distention of the elastic aortic arch through an increase in pressure (*potential energy of pressure*). The pressure change thus created is transmitted as a wave over the entire aorta and its many branches down to the capillaries, and causes successive expansions of more peripheral segments of the arterial tree. Obviously, this progressive expansion of the arterial wall from the aorta to the periphery must

be accompanied by a forward movement of blood so that arteries as far away as the dorsalis pedis are expanding before ventricular systole has terminated This pressure wave thus transmitted at a rate of 8 to 15 meters per second and the expansion and elongation of the arterial wall which it induces constitute the palpable or recordable arterial pulse

More precisely the velocity with which this pressure wave is transmitted peripherally depends on the distensibility characteristic of the vessels and on their degree of distention by internal pressures According to Sands[1] and Bazett et al [2] the normal velocity is less in the more distensible aorta (about 3 to 4 meters/sec) than in the muscular arteries of the limbs (about 7 to 14 meters/sec)

At this point it is well to be reminded of another established fact Whereas the pressure wave normally travels at a rate of 3 to 14 meters per second and produces an acceleration of blood flow along the whole arterial tree the actual velocity with which corpuscular elements move is much slower for example it averages only 18 cm /sec in the abdominal aorta and 14 or 15 cm /sec in the femoral arteries In other words whereas the pressure wave reaches the vessels of the foot within 0 2 to 0 3 second it requires 2 5 seconds (or several heart beats) for the corpuscles ejected into the aorta during any heart beat to reach the foot The reason for this may be clarified by the aid of the diagram in figure 2 As indicated in the crosshatched area all of the blood ejected during any systole is accommodated in the aortic reservoir This moves the blood within this segment to a more distal part of the arterial tree as indicated by the black area This in turn translocates blood to a third segment and so on The relation between the propagation of pressure and movement of the arterial blood column has been aptly compared to the rapid transmission of force through a row of billiard balls and the relatively slight onward movement which the row of balls undergoes

The Aortic Compression Chamber It is obvious that the elastic *aorta and to a lesser extent the arteries derived from it constitute* a continuous elastic chamber which takes up a considerable volume of blood under pressure during systolic ejection With the closure of the semilunar valves at the end of ventricular systole the pressure energy thus stored is gradually used to press blood out of the larger arteries through their branches and sub branches into the capillaries

Since the potential pressure energy is gradually converted into kinetic energy of flow the arterial pressure slowly declines during diastole It is for this reason that the elastic reservoir which insures a continuous capillary flow has been designated as the *compression chamber* of the arterial system

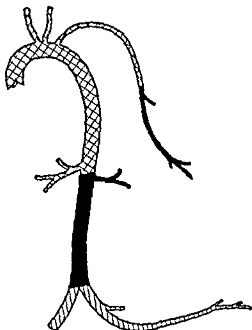


Fig —Diagram illustrating the translocation of blood in the aorta and some of its branches during three heart beats

The Pressure Pulse and Its Transformation in Transmission

By connecting highly responsive types of calibrated pressure recorders to various points in the arterial system as schematically indicated in figure 3 the details of the pressure changes during systole and diastole can be recorded at various points of the arterial system In such records the actual pressure existing at any moment of the cycle can be calculated and the rate of pressure transmission determined Figure 3 also illustrates the character and magnitude of the

pressure changes thus recorded from an aorta a radial and a femoral artery of the dog The whole pressure curve is designated the *pressure pulse* The maximal pressure reached during systole is the *systolic pressure* the minimal pressure realized at the end of diastole is the *diastolic pressure* and the numerical difference between these represents the *pulse pressure* The expansion of the vessels which the pressure pulse produces in any part of the arterial system is the *pulse*

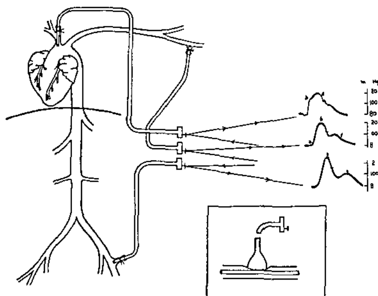


FIG 3—Diagram illustrating the principles of recording lateral pressure pulses from the aorta radial artery and femoral artery by optical manometers and the configuration of pressure pulses in these regions Insert diagram indicates procedure for recording pulsatile changes of arteries

A clear comprehension of these different terms and especially the differentiation between *pressure pulse* and *pulse pressure* is of the utmost importance in hemodynamic considerations to follow A glance at illustrations such as shown in figure 3 makes it apparent that the pressure pulses differ both as regards contour and systolic and diastolic values in different parts of the arterial tree

Under normal conditions the aortic pressure pulse rises sharply

(a–b) and after a high anacrotic shoulder (b), gradually rises to a rounded summit (b–c). The pressure then declines slightly during the latter third of systolic ejection (c–d) until closure of the semilunar valves, which is signaled by a sharp V-shaped incisura (e). During diastole (e–h) the pressure declines asymptotically except for a slight wave (f–g).

A pressure pulse recorded simultaneously from a peripheral artery such as the radial reveals a different form of pressure pulse. The beginning of the pulse is delayed; it rises less abruptly to a peaked and earlier summit (a–b). The systolic pressure taken at this point does not deviate greatly from that in the aorta, but it may be a little higher depending on the state of contraction of the muscular arteries. Having passed the peak, the pressure falls smoothly to a lower level during late systole (b–c) and early diastole (c–d) to the dicrotic notch (d) and thereafter acquires a prominent dicrotic wave (e–f) superimposed on its slow diastolic decline. The end diastolic pressure again is nearly equal to that of the aorta.

Similar changes take place in the femoral pressure pulse, but the rise is much more abrupt, the peak is sharper, and the systolic pressure reached exceeds that of the aorta, often by as much as 20 or 30 mm Hg. The diastolic decline of pressure during late systole (b–c) and early diastole (c–d) is also more abrupt, and the dicrotic notch and wave become more conspicuous than in records from the radial artery. It may be added that similar pressure pulses recorded from still more peripheral arteries such as the dorsalis pedis show even greater augmentation of the systolic pressure. Obviously a hemodynamic explanation is required which enables us to comprehend how an onward movement of blood can take place during systole when pressure is higher in the femoral artery than it is in the aorta. An answer is found in the fact that the pressure peak is reached later in the peripheral than in the central vessels; aortic pressure exceeds femoral pressure significantly during the early portion of systole, but a reverse pressure gradient temporarily supervenes during the latter part of systole which actually allows a backflow of blood toward the aorta.[3, 4]

The Phenomena of Damping and Wave Summation. A clear understanding of the problem demands an analysis of the hemodynamic phenomena which bring about temporal distortions of pressure pulses

in different arteries The transformation of the central to the peripheral pulse takes place chiefly through the operation of two major factors—damping and wave summation

1 The viscid blood in the elastic compression chamber acts as a liquid shock absorber by virtue of which minor abrupt pressure changes are smoothed away and the rates of pressure rise and fall are retarded This phenomenon is called *damping* As a result the

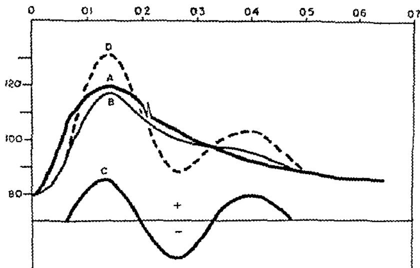


Fig 4 —Diagram illustrating the principles of damping and wave summation in the arterial system *A* aortic pressure pulse *B* changes in contour and amplitude due to damping *C* nature of rebound wave *D* summation of curves *B* and *C* Ordinate pressure in mm Hg Abscissa time in 0 1 sec

contour of the central pressure wave A is changed to that of wave B in figure 4

2 The forward impulse of the centrifugal pressure wave causes the blood column to rebound from regions of suddenly increasing resistance thus giving rise to a decrementing diphasic centripetal wave *such as illustrated in curve C of figure 4 Since both of these waves* are present in the same system of tubes they summate and cause a *resultant pressure pulse* such as is shown in curve D of figure 4 The

obviously has all the distinguishing characteristics of peripheral pulses exhibited in figure 3 the pressure continues to rise so that in the radial artery systolic pressure again equals that in the aorta and in the femoral and dorsalis pedis arteries it exceeds aortic pressure by 20 to 30 mm Hg Similarly a summation of the two waves causes the dicrotic notch and wave It is at present the consensus that the induced oscillation is a stationary pressure wave in the aorta produced by a positive rebound or reflection of the blood column from a point of rapidly increasing peripheral resistance which in effect reproduces the phenomena physically recognized in a closed tube but the locus of reflection is not agreed upon Recent observations[5] indicate that certainly under abnormal conditions and perhaps even under normal conditions[6] the induced oscillation may begin with a negative instead of a positive phase

Summarizing the sudden uptake of blood by the aorta during systole and the gradual reconversion of pressure energy to flow during diastole give rise to a characteristic pressure pulse in the aorta In its progressive transmission to peripheral branching arteries damping of this fundamental wave tends to obliterate the finer oscillations to retard the rate of pressure elevation and to reduce the pressure peak attained However the sudden impact causes a reflected pressure wave which summates with the fundamental wave in such a way that the peak pressure is restored to aortic systolic levels as in the radial or exceeds it as in the femoral In addition the diastolic limb is distorted by the accession of a negative dicrotic notch and a positive dicrotic wave As a result of the changes in the systolic portion of the peripheral pressure pulse a large volume of blood is first moved onward in the femoral artery during early systole but a part of this blood flows back during the latter period of systole

Human Systolic and Diastolic Pressures

The maximal and minimal pressures temporarily present in any artery—by definition the systolic and diastolic pressures—can now be recorded from accessible arteries by use of calibrated hypodermic manometers and they have even been recorded from the aorta through use of intra arterial catheters The e momentary pressures can of course be more conveniently measured by means of modern sphygmomanometers with the aid of proper technic[7] Comparison of in

direct and direct methods for determining arterial pressure in the brachial artery indicates that systolic and diastolic pressures can be determined with reasonable accuracy when the respective cuff pressures are read at the time that sounds appear and disappear in the cubital artery [7] The theoretical principles which underlie the use of *these sound phenomena as criteria of systolic and diastolic pressures* can be illustrated as in figure 5

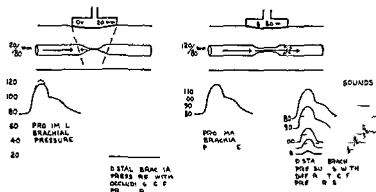


Fig 5 —Diagrams indicating theoretical foundation for determination of systolic and diastolic arterial pressures by palpation and auscultation To right dynamic conditions during complete occlusion of a compressed segment To left dynamic conditions in proximal and distal arteries including intensity of auscultatory sounds during serial decompression of artery Ordinates indicate intra arterial pressure except last column of numerals which indicates cuff pressures

As long as extra arterial pressure exceeds intra arterial systolic pressure (left diagram) the arterial segment under the compression cuff remains collapsed The arteries distal to the cuff empty and attain equilibrium with capillary and venous pressures at approximately 20 mm Hg Systolic pressure in the proximal artery rises a trifle above its normal value owing to an impact and reflection of pressure from the occluded vessel (Maltby and Wiggers[8])

When pressure in the cuff is allowed to fall progressively to or below intra arterial diastolic pressure (right diagram of fig 5) larger and larger segments of the proximal pressure pulse penetrate the compressed segment with the result that the distal arteries fill and the

peripheral pulse increases up to its normal amplitude Simultaneously hydraulic disturbances and/or changes in the arterial walls take place which are responsible for the sharp snapping auscultatory sounds of increasing then diminishing intensity (fig 5)

The dynamic mechanisms which create the Korotkoff sounds and the factors which determine their waxing and waning as extra arterial pressure falls to diastolic levels are not wholly understood The sharp snapping character of these sounds manifested alike on auscultation and registration[9] would seem to preclude their causation by turbulence peripheral to the cuff for turbulence usually give rise to murmurs not snapping sounds However turbulence may be a secondary factor when a distinct murmurish phase develops In 1919 Erlanger[10] presented experimental evidence which was consonant with the view that a water hammer effect is induced as blood rushes into the opening artery at high velocity Subsequent observations[11] on the movements of an isolated artery in a compression chamber brought to light evidence which seemed incompatible with such an explanation The fact that sounds arise in the distal end of the compressed vessel and start as soon as the compressed segment contains a small diastolic residuum led Erlanger to the conclusion that a vibratory state develops as soon as the transmitted wave passes through a partially filled unstretched vessel It increases as the diastolic residuum augments during decompression it diminishes when the vessel comes under tension and disappears completely when the vessel is fully opened Simultaneous registration of pulses peripheral to the compression chamber while an artery was being compressed revealed the existence of a series of sharp wavelets the most prominent of which was usually negative immediately ahead of the rising limb of the pulse The first Korotkoff sound became audible in the artery beyond the compression chamber simultaneously with the development of these wavelets As decompression proceeded the recorded wavelets increased in amplitude and complexity mounting on the anacrotic limb The snapping sounds were thus attributed to this so called pre anacrotic phenomenon later ascribed by Bramwell[1] to the breaking of a wave front In 1931 Frank and Wezler[13] redescribed the phenomenon and concluded that it is produced by longitudinal stretching of the arterial walls However Erlanger[14] in 1940 showed that this is not a necessary condition for development of the anacrotic phenomenon

The appearance of the pre-anacrotic vibrations superimposed on the pulse waves at various stages of decompression are shown in figure 6. Numerals have been arbitrarily assigned to indicate the relation of cuff pressures to assumed intra-arterial systolic/diastolic pressures of 120/80. As illustrated in the lowest curve, one of the early pulses to traverse a compressed segment of artery is characterized by a small negative dip and a very steep positive elevation followed by another dip and a few after-vibrations. These probably represent the first snapping sound which is heard. The pre-anacrotic vibrations are

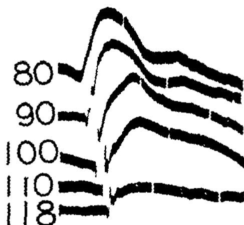


Fig. 6.—Series of actual pressure pulses showing pre-anacrotic phenomena followed by pressure pulse during various cuff pressures when arterial systolic and diastolic pressures are assumed to be 120 and 80 mm Hg respectively. Discussion in text.

succeeded by a slow pressure wave of small amplitude. As decompression proceeds (curves at 110–100 mm Hg extra-arterial pressure) the initial sharp negative oscillation is followed by steeper rises and larger after-vibrations apparently related to the increasing intensity of auscultatory sounds. They are followed by progressively larger pulses which start from higher and higher initial levels. As extra-arterial pressure (at about 90 mm Hg) approaches intra-arterial diastolic pressure, *the vibrations become coarser and mount higher on the* ascending limb. Presumably when extra-arterial pressure at 80 mm Hg equals intra-arterial diastolic pressure, the sharp sound vibrations

disappear and a pure pulse wave is recorded That such registrations actually incorporate both the transmitted pulse wave and the sounds heard on auscultation cannot be questioned Their interpretation is still subject to personal opinion The author is not wholly satisfied with Bramwell s breaker hypothesis [12] The very steep rise of pressure displayed is certainly suggestive of a water hammer effect [8]

Factors Affecting Systolic and Diastolic Pressures In normal individuals having a systolic pressure of approximately 120 mm Hg and a diastolic pressure of about 80 mm Hg the equilibrium of the arterial system is such that the rhythmic discharges of the left ventricle maintain a small reserve volume in the arterial compression chamber while the outflow from the arteries into the capillaries during systole and diastole equals the stroke volume Whenever this equilibrium is disturbed by changes in heart rate stroke volume peripheral resistance or arterial distensibility the peripheral outflow is disproportionate to the input until a new state of equilibrium has been established When this has been attained the normal relation of systolic to diastolic pressure is altered The nature of the changes is studied to best advantage in artificial circulation schemes in which one factor can be altered at a time Such studies illustrated in figure 7 have shown that an increase in heart rate elevates diastolic pressure more than systolic thus reducing the pulse pressure increase in stroke volume raises systolic pressure more than diastolic thereby increasing the pulse pressure Augmentation of peripheral resistance elevates diastolic pressure more than systolic until diastolic distensibility begins to diminish drastically then systolic pressure rises progressively faster than diastolic until the pulse pressure actually exceeds the normal As illustrated by the solid lines in figure 8 the change in trend normally occurs approximately at levels of 100 mm Hg of diastolic pressure but considerable elevation of diastolic pressure (to approximately 150 mm Hg) is required before the pulse pressure exceeds that existing at normal diastolic levels If however the distensibility of the arterial system is reduced by pathologic processes (as in arteriosclerosis and perhaps through functional changes in arterial walls) the pulse pressure amplitude begins to increase at lower diastolic pressure levels This is illustrated by the solid plus the dotted lines in figure 8

The dynamic changes responsible for the relative changes in systolic

and diastolic pressure and therefore in pulse pressure amplitude deserve a more complete analysis. Comprehensible theoretical ex-

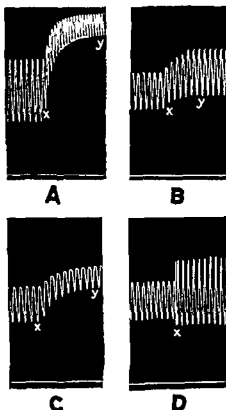


FIG 7.—Records obtained from artificial circulation model illustrating effects on systolic and diastolic pressure during and after (x–y) alteration of various factors separately. *A*, effect of increasing heart rate. *B*, effect of increasing stroke volume. *C*, effect of increasing peripheral resistance within constant ranges of arterial distensibility. *D*, effect of reducing distensibility of arterial system.

planations can be based on postulations which involve balances between the systolic input into the aorta under different degrees of distention and the relative outflow from all branches of the arterial tree

during systole and diastole An illustration to which such an analysis fortuitously applies may be given Suppose the heart beating at 75 beats per minute delivers stroke volumes of 70 cc each into an elastic aorta Sufficient blood is moved along so that we may assume a run

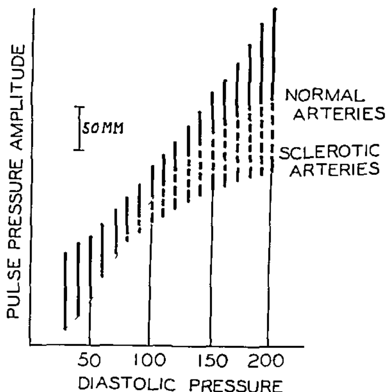


FIG 8 —Diagram illustrating the anticipated changes in pulse pressure amplitude at different diastolic pressures in normal arteries (solid lines) and in sclerotic arteries (solid plus dash lines) Discussion in text

off from the whole arterial tree of 25 cc during systole and 45 cc during diastole If stroke volume peripheral resistance and aortic distensibility remain the same while the heart rate increases to 90 beats per minute *the reserve volume in the arterial system becomes* greater and diastolic pressure is elevated When an equilibrium has been attained relatively more blood leaves the peripheral arterial

system during systole owing to the elevation of mean systolic pressure and less runoff during diastole owing to the abbreviation of this period Since more energy is converted to flow during systole and less proportionately during diastole systolic pressure is raised less than diastolic pressure Hemodynamic studies[15] have shown however that this type of logical analysis does not hold in the case of other determinants of systolic and diastolic pressures and indeed is not the basic explanation for effects produced by heart rate changes The dynamic considerations even fail in simple circulation schema in which flow from a single tube with a controllable terminal resistance is used For example when heart rate stroke volume and arterial distensibility all remain constant an increase in peripheral resistance causes a relatively greater elevation of diastolic pressure and a smaller pulse pressure According to this concept one would need to postulate a redistribution of peripheral efflux so that systolic outflow becomes relatively greater and diastolic outflow relatively less than under control conditions It has been shown in circulation models[15] that contrary changes occur systolic runoff is relatively reduced a trifle and diastolic runoff correspondingly increased The situation becomes even more complicated when the runoff from the arterial tree occurs through numerous branches with widely differing lengths and different coefficients of elasticity

A better explanation is based on the relation which exists between the total volume of the arterial tree and the systolic uptake during ventricular contraction As long as the volume elasticity coefficient remains relatively constant this is expressed by the formula

$$\frac{dp}{dv} V = K$$

in which V is the actual volume of the elastic arterial system dv the sudden increment in its volume and dp the sudden increment of pressure produced Translated the formula can be written $\frac{\text{pulse pressure}}{\text{stroke volume}} \times$ diastolic volume remains constant

During cardiac acceleration the stroke volume remains unchanged but since the diastolic volume of the arterial system increases pulse pressure must necessarily decrease to balance the equation

With increased systolic discharge the stroke volume increases more

than the diastolic volume of the arterial system and pulse pressure must necessarily increase to balance the equation

With augmented peripheral resistance to outflow the diastolic volume increases while the systolic discharge remains constant As long as the coefficient of elasticity remains unchanged the pulse pressure decreases Under greater degrees of distention the distensibility of the arterial system decreases rapidly so that greater pressure increments are required to stretch the walls and accommodate the normal systolic discharge Therefore systolic pressure mounts progressively with increasing peripheral resistance until the pulse pressure exceeds the normal (fig 8) Similar supernormal pulse pressures can, however develop at considerably lower diastolic pressures when the distensibility of arteries has been reduced When pulse rate stroke volume and peripheral resistance remain unchanged reduction in aortic distensibility per se causes a slight decline of diastolic pressure and a considerable rise of systolic pressure with pronounced increase in pulse pressure (fig 7)

The Clinical Importance of Arterial Pulse Tracings

The *pulse* represents the changes in diameter of vessels produced by internal changes in pulse pressure Since a lag in the response of arterial walls to internal pressures called hysteresis has been observed experimentally in excised arterial strips [16] and in the aorta in situ following protracted and drastic changes in diastolic distention [17] the question arises whether the pulse recorded from large arteries faithfully depicts the form and magnitude of the pressure pulse There is no good evidence that hysteresis operates under stabilized conditions Simultaneous registrations from the interior and exterior of a vessel give curves which are identical within the limits of measurement the finer vibrations which occur during isometric contraction and during closure of the semilunar valves are accurately inscribed on central pulse tracings at proper pressure levels

Arterial pulses can be recorded accurately from superficial arteries by firmly pressing a small funnel over an artery and connecting this with an optical recorder (see insert fig 3) Registration from deeper arteries such as the radial requires the use of special instruments called sphygmographs the principles and operation of which are described elsewhere [18]

Typical subclavian and radial pulses from a normal subject are reproduced in figure 9. It will be noted that their contours conform essentially to that of pressure pulses depicted in figure 3.

Clinical Information Derived from Central Pulses. The durations of systole and diastole and of the whole cycle give information regarding temporal events of the cardiac cycle. Normally, a definite and almost constant linear relationship exists between total systole and cycle length. This is the so called S/C ratio. Graphs and formulae

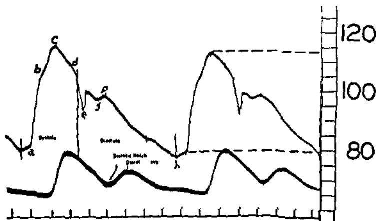


Fig 9.—Human subclavian and radial pulses showing correspondence of contours with those of intra arterial pressure pulses. Compare letters a–h in these records with those in figure 3. By placing systolic and diastolic pressures determined by sphygmomanometry to top and bottom of such curves an ordinate scale on left can be constructed. Discussion in text.

for the expected average durations of systole at different heart rates have been constructed by different investigators.[19, 20] Deviations from the normal standard can be measured. A permanent increase in the period of systole more than 0.2 second beyond the figure characteristic for a given heart rate suggests that the diastolic size of the ventricle is increased. This may be caused by a greater venous return or through accumulation of blood during compensated pathologic conditions. Excessive abbreviation of systole when the heart rate is rapid is frequently indicative of a predominant accelerator nervous or adrenergic humoral influence. Systole is also decreased

during myocardial failure such as supervenes during anoxia atrial fibrillation valvular insufficiency or hypertension In such cases abbreviation of ejection is usually associated with an elevation of venous pressure and increase in diastolic size

The contour of the central pulse gives useful information with regard to the discharge process of the left ventricle under abnormal conditions Several typical deviations from the normal are shown in figure 10 When peripheral resistance is high and the aorta is normally distensible the pulse exhibits an initial steep rise followed by a rising plateau until the incisura When aortic resistance is low while the

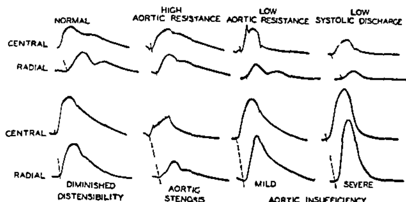


FIG 10 —Illustrations of changes in contour and amplitude of subclavian and radial pulses under abnormal cardiovascular conditions Discussion in text Note changes in transmission rates

stroke volume remains good the pulse curve displays a preliminary peak due to a momentary fling of blood in the lax arterial system This is followed by a lower systolic summit succeeded by a rapid decline and a deep incisural drop to a low diastolic level When the stroke volume is small the pulse displays a smooth rounded curve during systole and a low flat segment during diastole Diminished distensibility of the aorta is characterized by a rapid ascent of a large pulse wave a high incisura and a gradual asymptotic decline during diastole Lesions of the aortic valves cause distinctive pulse patterns Aortic stenosis results in a small pulse initiated by a brief sharp rise which is succeeded by a sharp anacrotic incisura This in turn is followed by a slowly rising systolic plateau upon which murmur vibra

tions are superimposed Aortic regurgitation is always accompanied by a large pulse for the diastolic pre sure is low and the pulse pressure large The magnitude of the regurgitation is generally reflected in the diastolic decline in small leaks the decline occurs gradually during diastole in large leaks it takes place immediately after the incisura The reasons for these changes are discussed in Chapter III

Clinical Value of Radial and Femoral Pulses While the registration or palpation of these pul es offers a convenient method for estimating heart rate and for discovering or even identifying arrhythmias it should be apparent that their *value in estimating performance of the* left ventricle is decidedly reduced by virtue of physical changes in transmission of the pressure pulse Nevertheless significant changes accompany some of the conditions discussed above For example in arteriosclerosis the approach to a more rigid state allows a more rapid and faithful transmi sion of pre ure to the periphery so that as illustrated in figure 10 a definite incisura may be present In states of high peripheral resistance or reduced cardiac output the curves are chiefly characterized by changes in their amplitude In aortic stenosis the rise of the ascending limb is very much retarded and may display an anacrotic notch The chief characteristics of severe aortic insufficiency consist of a rapid ri e of pressure to a high maximum giving rise to the palpatory sensation described as water hammer and a rapid decline of pre sure with abolition of the dicrotic wave decribed as the palpatory sensation of collapse The water hammer and collap ing features together constitute the Corrigan pulse

Reconstructed Pressure Pulses in Man Obviously the pul e curves just described give only the contour of pres ure variations within an artery they are devoid of ordinate values If at the time that central pulse tracings are recorded systolic and diastolic pressures are meas ured in the brachial artery no great error is incurred in placing these values at the summit and foot of an arterial pulse and subdividing these pre sure values proportionately over the span This procedure is shown in figure 11 In this way a pressure pul e such as could be recorded directly from the interior of an artery can be recon tructed with a reasonable degree of fidelity

From such recon tructions in which the ordinate scale is projected to zero it is po sible to make a number of constructions from which important dynamic information can be derived For instance a pres

sure pulse (schematically shown in figure 11) may be integrated to determine mean pressure (P_m) during any cycle by measuring the pressure area under such a curve and determining its average height Since such integration takes cognizance of the contour of the pressure pulse the mean pressure so determined is more reliable than various proposed formulations which arbitrarily estimate P_m as one half systolic + diastolic pressure or diastolic pressure + $\frac{1}{3}$ pulse pressure etc Obviously such mean pressure is only a theoretic one

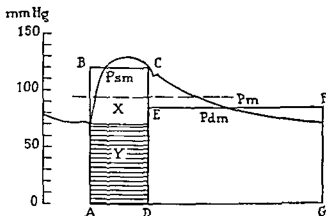


FIG 11 —Diagram illustrating the integration of a central pressure pulse for accurate determinations of mean cyclic pressure (P_m) mean systolic pressure (P_{sm}) mean diastolic pressure (P_{dm}) and the fractions of systolic mean pressure which represent static effort (Y) and dynamic effort (X) Discussion in text (After C J Wiggers Physiology of Shock courtesy of the Commonwealth Fund)

but it is highly important in calculating peripheral resistance (see below) It is also possible to determine the mean pressure which exists during systole (P_{sm}) or diastole (P_{dm}) respectively by converting the pressure curve during these phases into two theoretic rectangles (A B C D and D E F G) Under certain conditions a knowledge of the systolic and diastolic mean pressures is very important The mean diastolic pressure is a dominant determinant of coronary flow whereas the mean systolic pressure (P_{sm}) rather than the mean cyclic pressure (P_m) should be used in calculations of cardiac work In arteriosclerosis aortic insufficiency and hypertension P_{sm} greatly exceeds P_{dm} indi

cating that the runoff from the arterial system is much greater during systole than during diastole The capillary pulse often observed in these conditions is thus explained by the altered dynamics of the circulation Unfortunately changes from normal P_m/P_{dm} ratios cannot be used as a quantitative index of the relative influx into capillaries during systole and diastole Apparently different lengths and diameters of arteries leading from the aorta to capillaries affect regional outflows through variable damping and peripheral pressure chamber effects [15]

The pressures during systole can again be divided into components illustrated by the areas X and Y of figure 11 The total pressure energy represented by area Y equals the pressure energy that the left ventricle is required to expend as static effort in maintaining pressure at a diastolic level If the ventricle should develop only sufficient pressure for this purpose as frequently happens in early premature contractions no ejection could occur (see Chapter III) The pressure developed over and above this (area X) on the contrary is expended in the forward movement of blood Consequently the quotient $\frac{\text{area X}}{\text{area Y}}$ can be recorded as an index of the economy of effort during ejection (Wiggers and Katz [1]) While such a quotient is not equivalent to the mechanical efficiency of the left ventricle (work energy total energy) studies on the energetics of muscular contractions suggest that it may under varying dynamic conditions alter directionally if not quantitatively as the mechanical efficiency

Estimation of Stroke Volume and Cardiac Output Many attempts have been made to utilize data supplied by pressure pulses for estimation of stroke volume and through multiplication by heart rate of cardiac output per minute The simplest criterion involves the use of pulse pressure In 1904 Erlanger and Hooker[22] suggested that the pulse pressure is dominantly affected by changes in stroke volume thus the product of pulse pressure and heart rate should serve as a fair index of directional changes in cardiac output While this criterion may have some predictive value when its use is limited to the study of changes in cardiac output in the same subject the current consensus is that it is not reliable in comparing the cardiac outputs of different individuals because the arterial distensibility encountered in different individuals varies so greatly [1] Attempts to take cognizance of the

distensibility characteristic of the aorta by relating pulse pressure to diastolic mean or some arbitrary value (e g $Pd + \frac{PP}{(\bar{P})}$ $\frac{PP}{(\bar{P})}$ $\frac{PP}{\frac{1}{2} Pd + \bar{P}}$) have also not proved successful[23]

A number of investigators have made serious efforts to employ other information supplied by pressure pulses in the calculation of stroke volume A discussion of these procedures would carry us too far afield A summary can be found elsewhere[20] The technic requires specialized training to avoid pitfalls Most important comparisons of cardiac output by these methods and use of the Fick principle have not been found consistently favorable Those who report consistent results admit that the integration process cannot be applied to abnormal types of pressure contours and finally the procedure is as yet not applicable to human beings[23] (See also Alexander[6])

The Dynamics of Hypertension

Clinical studies strongly support the view that essential hypertension is not basically accounted for through increase in heart rate stroke volume or blood viscosity hence the inference based on Poiseuille's law that increased peripheral resistance must necessarily be the primary factor

The Concept of Peripheral Resistance Resistance to flow of blood is encountered throughout the arterial tree To judge from the decline in mean cyclic pressure from the aorta to the terminal branches of the arterial tree in normal subjects this resistance according to Frank amounts to about 20 per cent of the total resistance However the minute vessel including arterioles metarterioles and capillaries constitute the chief areas of changing peripheral resistance The adjective peripheral therefore refers solely to the minute distal vessels of the arterial tree regardless of whether they are located in the interior or on the surface of the body Some confusion on this point occasionally arises because in clinical practice circulation in superficial vessels is also referred to as the peripheral circulation

Peripheral resistance is determined by all factors which tend to impede the flow of blood from branches of the arterial tree These include (a) passive factors such as the equilibrium between intra and extravascular pressures and the resistance offered by venous pres

sure di tal to capillaries and (b) active factors such as changes in the caliber of arterioles produced by vasomotor action Physically and according to Poiseuille s law resistance is determined by the char acteristic of the tube (length/diameter and blood viscosity (1)) In applying Poiseuille s law derived from the study of flow through rigid tubes to pul ating flows in elastic systems such as the arteries a number of re ervations must be made in calculations According to formulation peripheral resistance is u ually treated as though the diameter and length of minute vessels remain es entially constant with increasing pre ure and during ch inges of pressure in the cardiac cycle Actually direct microscopic ob ervations indicate that ves els expand and retract passively with changes in pressure They have also revealed that the minute ves els of many regions undergo in termittent changes in size—sometimes to the point of complete ob literation The fact that this intermittence occurs out of phase in different regions probably accounts for the relatively con tant arterial pressure maintained in the larger arteries When these variations be come synchronized they give rise to the well known vasomotor or Traube Hering waves of arterial pressure

In order to simplify hemodynamic analy es mall arteries and arterioles have generally been treated as though they branched di chotomously into capillaries and the resist ince has been computed from the respective lengths and diameters of succe ive linear seg ments Such a scheme fails to take cognizance of large and small arteriovenous shunts the capillary hunts de cribed by Chambers and Zweifach in viscera the numerous inu es in the pleen liver and heart etc The possibility hould be kept in mind that closure of arteriovenous shunts and contraction of precapillary phincters rather than active change in the arterioles leading directly into capillaries constitute the true stopcocks of the circulation The viscosity factor which enters into Poiseuille s equation is a tricky component to eval uate in the body The vi cosity of blood predetermined in vitro is entirely different from that of the same blood flowing through capil laries of an organ This i in part due to effects that the small di ameters of capillaries have on visco ity and in part to the inter change of pl ma which takes place in the e regions Al o the red corpuscles alter in size in their pa age through capillaries as a result of the interchange of gases The concentration of corpuscles which

takes place particularly in the kidney after extraction of the glomerular filtrate is a vivid example of changes in viscosity which take place within the capillaries themselves

It is therefore not surprising that most observers have failed to find a linear relation between pressure and flow in most organs studied including skeletal muscle kidney and lungs (For references see Wiggers [4]) According to Green [5] the minute vessels may dilate passively or new capillaries and A–V anastomoses may open as arterial pressure elevates from low to high levels The effect which these passive changes have on calculations of peripheral resistance must be established before vasomotor action can be inferred from pressure/flow relations

The foregoing discussion should make it obvious that changes in peripheral resistance in any region cannot be derived from simple application of Poiseuille s law Nor can estimates of changes in viscosity be deduced by juggling the factors in Poiseuille s equation Many tyros in hemodynamic investigation have fallen into these traps

The Concept of Total Peripheral Resistance The resistance of the arterial system cannot be calculated as in a branching and rebranching tube in which all of the liquid flows through a single set of terminal vessels of minute size The architecture of the arterial tree is such that organs and tissues are supplied through many parallel circuits each with its own resistance A mechanical concept of such shunts each with its own resistance (r_1 r_2 r_3 etc) is schematized in the diagram of figure 12

The term total peripheral resistance (TPR) translated from the German *Gesamt Widerstandt* signifies the resultant resistance to efflux from many parallel circuits such as exist in the body Theoretically such a total resistance may be calculated as in electric circuits

$$\frac{1}{TPR} = \frac{1}{r_1} + \frac{1}{r_2} + \frac{1}{r_3} + \qquad \frac{1}{r}$$

Since, under stabilized conditions the efflux from all of these circuits over a certain time interval equals the cardiac output over the same period TPR can be expressed as mean aortic pressure divided by cardiac output Such calculations have been used extensively in attempts to differentiate changes in arterial pressure due to cardiac

or total peripheral resistance factors They must however be used with a keen recognition of their limitations The resultant resistances

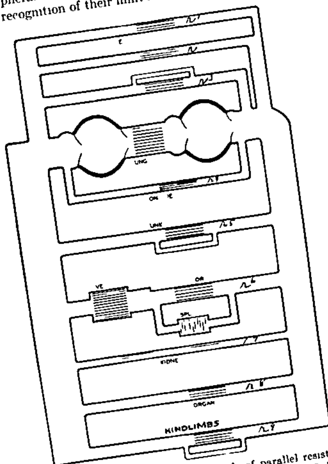


Fig 12 —Diagram illustrating the principle of parallel resistances in the circulatory system (After C J Wiggers Bull N Y Acad Med courtesy of New York Academy of Medicine)

in numerous parallel circuits do not indicate that similar directional changes are necessarily taking place in all vascular territories or organs the resistance may indeed increase in some regions and decrease

in others While it is the consensus that such calculations of TPR in the presence of moderate changes in mean arterial pressure do indicate directional changes it is not a necessary inference that such changes are occasioned by vasomotor action Finally the fact that TPR can be expressed in numerical units perhaps gives a false sense of quantitation which does not exist

Units of Resistance In electrical physics the ratio of electromotive force to current flow is designated by a unit known as the ohm It has seemed desirable to have similar hydraulic units of resistance The most widely used formula reduces all values to c g s units

$$TPR = \frac{\text{mean pressure} \times \text{mm Hg} \times 13.6 \times 980}{\textit{cardiac output (cc/sec)}}$$

$$= \frac{\text{mean pressure} \times 1332}{\text{cardiac output (cc/sec)}} = \text{dynes sec/cm}^5$$

The author has designated this as the absolute unit (a u) but owing to its small magnitude a large absolute unit (A U) equaling 1000 a u seems more serviceable in the study of territorial resistances [4] In order to avoid calculation of mm Hg into absolute units Green and his associates [5] suggested as a unit PRU an abbreviation for the term peripheral resistance unit This is defined as

$$\frac{\text{mean arterial pressure (mm Hg)}}{\text{flow in cc/min}}$$

This unit is however so large that TPR would equal approximately 1/60 PRU Bazett has suggested the formula

$$R = 3\,\frac{\text{mean arterial pressure (mm Hg)}}{\text{cardiac index}}$$

which gives a normal value of about 100 However it has been questioned whether it is desirable to introduce surface area into such equations A unit suitable for all occasions has so far not been evolved (See discussion Wiggers [4])

The Interpretation of Changes in Pressure Pulses and Pulse Pressure of Hypertension If as is generally conceded hypertension is chiefly occasioned by increase in peripheral resistance, the pulse pressure would be expected to diminish at least until diastolic pressure ex

ceeds 100 mm Hg Actually clinical studies have revealed that systolic pressure is elevated comparatively more than diastolic and that the pulse pressure exceeds normal values The explanation would appear to be that the processes which cause contraction of the arterioles also act to reduce the extensibility of larger arteries comprising the compression chamber and thus virtually act as milder forms of arteriosclerosis The following evidence has been brought forward on previous occasions [6, 47] to support this theory (1) If we compute total peripheral resistance (TPR) in normal subjects and in patients with varying degrees of hypertension the curve of TPR and mean blood pressure are not parallel many discrepancies exist between the degree of hypertension and calculated TPR Thus cases are found in which a high mean pressure is associated with a nearly normal TPR and others in which a relatively slight elevation of mean pressure shows a high TPR (2) If the central and peripheral arterial pulses are recorded from patients having diastolic pressures over 90 mm Hg and a high systolic pressure they fail to show the contour changes characteristic of an increase in peripheral resistance alone All have earmarks of pressures transmitted over less distensible tubes as illustrated in figure 10 (3) Experimental evidence has been adduced that acute hypertension produced by vasoconstrictor drugs is accompanied by a reduction in the caliber and distensibility of the aorta [1]

If these hemodynamic considerations are correct the common interpretation of the significance of diastolic pressure readings in hypertensive states requires revision It is a common impression that elevation of systolic pressure even though considerable is not too serious as long as diastolic pressure remains low According to hemodynamic laws and the evidence which has been submitted it would seem to indicate a reduction of arterial distensibility i e either development of arteriosclerotic changes or diminution of aortic distensibility due to functional mechanisms

The real reason why a high diastolic pressure is apparently more unfavorable for the left ventricle can be clarified by again referring to figure 11 It is obvious that the higher the diastolic pressure the greater the static effort (X) which must be developed before blood is ejected into the aorta Consequently the question presents itself whether the left ventricle contracting against a higher diastolic pres

sure operates less efficiently than under normal conditions To study this problem Wright and his associates[73] compared the economy of effort in hearts of 81 normal and 54 hypertensive subjects by determining the ratio of the static and dynamic components according to the method outlined Their survey revealed that the economy of effort in hearts of normal medical students instructors and attendants ranges from 0 215 to 0 880 with a median of 0 428 Hypertensive patients showed a wider range of the index namely from 0 220 to 1 030 However 70 per cent had an index above 0 428 the median of the normal group The encouraging fact emerges from such studies that a large proportion of hypertensives display an economy of effort index which equals or exceeds that of normal subjects Analyzed with respect to age persons 50 years of age or more tend to have a better economy of effort index than younger hypertensives

Summary

1 The factors concerned with the flow of blood in the arterial system are basically expressed by Poiseuille s law but this formulation describes the dynamics of pulsating streams in elastic vessels only partially

2 Each ventricular systole forces blood into an already filled and stretched aorta partly by moving the existing column peripherally and partly by further distension of the aorta and its branches During diastole the gradual recoil of the elastic walls causes the flow of blood to continue out of the arterial system through arterioles into capillaries The steady flow through capillaries is thus achieved by the *compression chamber function* of the aorta and the volume of capillary flow is determined by vasomotor changes in arterioles which act as the *stopcocks of the circulation*

3 The phasic changes of pressure during systole and diastole—directly recordable from the arterial system—are called the *pulse pressure* The highest and lowest pressures momentarily reached during systole and diastole respectively are by definition the systolic and diastolic pressures and their difference is the *pulse pressure* The changes in the diameters of large arteries which conform to internal pressure changes constitute the *pulse*

4 The contour of the central pressure pulse is altered in its transmission to peripheral arteries such as the radial and femoral by

(a) damping of the basic transmitted pressure wave and (b) by summation with a diphasic reflected wave The former tends to reduce and the latter to raise systolic pressure over that in the aorta

5 The mechanism of the Korotkoff sounds commonly employed as criteria in the estimation of human arterial pressure is discussed

6 The relative changes in systolic and diastolic pressures often allow inferences as to the cause of blood pressure readings which deviate from normal standards Thus assuming a normal state of arterial distensibility pulse pressure increases as a result of augmented stroke volume it is reduced by cardiac acceleration and up to diastolic pressure of approximately 100 mm Hg by increased peripheral resistance Above this diastolic pressure and at lower pressures when aortic distensibility is reduced pulse pressure increases steadily The reasons for these effects are given

7 Properly recorded pulses from central arteries permit important deductions regarding cardiac behavior (a) by calculation of the temporal relations of systole to cycle length (S/C ratio) and (b) by distinctive changes in pulse contours The latter are described and illustrated

8 Central pulses can be converted to central pressure pulses with reasonable accuracy by placing systolic and diastolic pressure readings obtained from the brachial artery as ordinates for the summits and troughs of pressure curves Through integration of such curves mean cyclic mean systolic and mean diastolic pressures can be estimated The value of each of these in hemodynamic analysis is discussed Reconstructed pressure pulses also enable one to evaluate the economy of left ventricular effort

9 The architecture of the arterial system is such that many shunt circuits are derived from the aorta before its bifurcation into the iliac arteries Each of these circuits has its variable regional resistance The resultant or so called *total peripheral resistance* (TPR) is determined by variations in the various regional resistance A number of units of resistance are defined and cautions are given regarding the possibility of drawing unwarranted interpretations from numerical data thus derived

10 The hemodynamic principles discussed are applied to the problem of human hypertension This condition is not satisfactorily characterized as a disorder of augmented total peripheral resistance

reduced distensibility of large arteries organic or functional in nature, must be assumed to account for the characteristic changes in arterial pulses and pulse pressures The encouraging fact emerges that a large proportion of hypertensives particularly in the older age groups maintain an economy of effort of the left ventricle which equals or exceeds that of normal subjects

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CHAPTER II

Determinants of Cardiac Performance*

DURING the past 50 years progress in the study of heart disease has been achieved over different pathways.[1] Among these is the clinical application of instrumentations and technics originally designed in and limited to physiologic laboratories. Since my entry into medical school in 1901 I have witnessed the successive employment of sphygmographs, phlebographs, apex beat recorders, sphygmomanometers, plethysmographs, roentgenographs, electrocardiographs and phonocardiographs. Some of these have not survived the dictates of experimental fashions and are known to the present generation only as museum pieces or text figures,[2] if at all. They were retired from the armamentarium of clinicians because the information gained did not appear commensurate with the time and effort required for their proper use. With the development of high fidelity pressure recorders in laboratories and the demonstrated safety of arterial punctures[3] and cardiac catheterization in hospitals[4] we have entered an era in which circulatory derangements are being intensively studied through the interpretation of cardiac outputs and of pressure pulses recorded directly from the cardiac chambers and large vessels. The interpretation of circulatory dynamics by such procedures requires not only a comparison of data from human subjects in health and disease but also the utilization of information derived from more controllable experiments on animals. We can obviously not hope to comprehend the processes through which organisms die unless we understand the mechanisms which keep them alive.

The purposes of this review are (1) to restate briefly some important experimental results on cardiac performance, (2) to re-examine concisely the deductions, theories and concepts of cardiac behavior to

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which they have given rise and (3) to attempt a resynthesis of evidence into a modern physiologic concept of myocardial regulation Such a process of modernization involves a divorcement of factual data from theories and the integration of successive discoveries with classical ones of the past When this is done it frequently happens as in this instance that very old laws of cardiac behavior have merely been given more extended applications rather than that essentially new ones have been discovered

Three Classic Discoveries

1 In 1869 a young American Dr H P Bowditch undertook the study of physiology in Ludwig s laboratory in Leipzig His investigation on the apex of the frog s ventricle published in 1871[5] has become a classic in physiology He showed that if the condition of the heart muscle remains unaltered the contractions remain equal regardless of the strength of stimuli applied As Ranvier[6] expressed it the heart s motto is all or none The paradox that the ventricles can obviously alter the vigor of their contractions under normal as well as pathologic conditions was explained by another observation in the same investigation namely that excitation of the resting frog s ventricle by successive shocks *of the same intensity at short intervals* results in a progressive increase in amplitude of contractions The phenomena called treppe or staircase is obviously occasioned by the fact that each stimulus exerts a beneficial after-effect on the responsiveness of cardiac muscle

Summarizing the law of all or none implies that cardiac muscle either does not contract at all or responds to the fullest extent but the magnitude of the all or none response is determined by the inherent condition of the muscle

2 In 1884 Howell and Donaldson[7] presented unequivocal evidence that the dog s heart has intrinsic mechanisms by which its output is nicely adjusted to the venous input Using the Newell Martin heart lung preparation it was found that augmentation of venous inflow to a heart weighing 76 Gm caused the cardiac output to increase from 480 to 1964 cc per minute the stroke volume from 5 2 to 21 6 cc and the right atrial pressure from 10 to 60 cm of blood The compensation for increasing volumes of venous return was not quite perfect however increases in output of the left ventricle lagged progressively

behind the available supply of blood in the venous reservoirs Upon reducing venous inflow so that atrial pressure fell to the original level of 10 cm of blood cardiac output dropped to 400 cc and the stroke volume to 2 38 cc which indicated that the performance had deteriorated slightly after a short period of strain

3 In 1895, O Frank[8] published his investigations on the dynamics of heart muscle His object was to correlate as far as possible the mechanical reactions of cardiac muscle with the well known responses of skeletal muscle previously established by A Fick J von Kries and Blix It should be recalled that these investigators had established a relationship between the force of contraction and the degree of stretch and tension under which skeletal muscles were placed previous to stimulation that is the so called initial length and tension Frank recorded isometric and isotonic contractions of the frog s atria and ventricle during various degrees of diastolic filling and pressure He found that within limits stepwise increases in diastolic volume and pressure just before contraction—hereafter called the *presystolic volume and pressure*—determine the magnitude of the all or none response These studies emphasized that the cardiac response to artificial or natural excitation is determined wholly by hemodynamic events which precede excitation

Years of experimentation have not only confirmed the basic laws of cardiac behavior founded upon these observations but they have also elucidated the many variables which tend to obscure their operation in the control of the mammalian heart under normal and pathologic conditions

The Law of Uniformity of Behavior

In 1906 Y Henderson[9] succeeded in improving previously used plethysmographic technics sufficiently to establish patterns of ventricular filling and emptying under different circulatory conditions A study of cardiometric records led Henderson and his associates[9] to the conclusions (1) that the ventricles have a fixed pattern of relaxation which determines their diastolic capacity as long as the venous supply is at normal levels and (2) that further increase in venous supply cannot augment ventricular filling and systolic discharge Such a concept set an extremely low limit to the cardiac response to increasing initial tension and length According to this view

also the only way in which greater volumes of venous blood could be pumped to the aorta would be through an increase in heart rate. According to his "law of uniformity of behavior," cardiac output increases progressively up to rates of 180 per minute, thereafter becoming stationary and during extreme tachycardia diminishing rapidly.

A reappraisal of Henderson's work indicates that his analysis of ventricular volume curves gives a valuable geometric plan for evaluating the effect of cycle length on systolic discharge and cardiac output, but his conclusion that increased venous return cannot augment ventricular filling does not seem to have been supported by valid experimental evidence. Henderson was unquestionably correct in his deduction that ventricular filling occurs largely in early diastole as a result of A-V pressure differences, but he underestimated the additional quantity of blood that the atria inject into the ventricles, partly because the slower beats in his experiments were obtained during vagus stimulation and therefore associated with depression of atrial contraction.

The Applicability of Laws of Initial Tension and Length to Mammalian Hearts

In 1914 the writer[10] reported experiments which demonstrated that every increase or decrease in volume of blood returning to the right atrium simultaneously alters the initial tension, height, and contour of the right intraventricular pressure curve. These experiments were the first to demonstrate that the reactions established for the frog's ventricle are also applicable to the naturally beating right ventricle of dogs. In brief, the conclusion was reached that the gradient of the isometric pressure rise and the peak systolic pressure are determined by changes in the presystolic tension, as long as marked changes in inherent contractility are not simultaneously produced by experimental procedures.

Concurrently and quite independently other investigators, notably Starling and his associates[11] and Straub,[12] investigated the effect of changes in presystolic tension and length on responses of isolated hearts. Since the work of Starling and his group has aroused the greatest attention in relation to clinical studies, a reappraisal of their investigations and conclusions should be of timely interest. These investigators

utilized their well known heart lung preparation[13] which was designed to control heart rate mean arterial pressure and venous inflow, and to vary any one of these factors at a time This was of signal importance despite the facts that the individual factors cannot be controlled as independently as the British investigators believed and that the dynamic conditions under which the heart operates deviate somewhat from those which exist in the body [14-7] The important results and conclusions pertinent to our discussion can be summarized as follows

1 When arterial resistance and venous inflow were kept constant —within limits of the preparation—variations in heart rate from 60 to 160 per minute caused no significant changes in cardiac output per minute (Markwalder and Starling[11]) a conclusion diametrically opposed to that of Henderson and his associates [9] The inference was drawn—and later it was supported in a measure by registration of volume curves—that ventricular filling is not dominated by a fixed pattern of relaxation and elastic resistance to filling pressures (Patterson Piper and Starling[11])

2 At constant heart rate and mean arterial pressure progressive augmentation of venous inflow caused progressive increases in diastolic size (stretch) systolic discharge and cardiac output per minute up to a critical atrial pressure (compensation) Beyond this systolic discharge and cardiac output decreased (decompensation) These results were interpreted as follows A compensatory increase in stroke volumes takes place *as long as the ventricles can undergo additional distention* When no further distention is possible owing to limitations imposed by the elastic ventricular stretch or the restraining action of the pericardium [13] the rapidly increasing presystolic tension exerted on individual fibers hinders the development of contractile force and systolic discharge diminishes (Patterson Piper and Starling[11])

3 During the compensatory state that is while cardiac output increased with augmenting venous supply—pressures rose *pari passu* in both atria slowly at first and thereafter at a progressively increasing rate During the stage of decompensation (when cardiac output of the left ventricle began to decline) pressure rose rapidly in the right atrium but fell in the left (right heart failure) (Patterson and associates[11])

4 The fatigued or depressed heart could have an output equal to

that of a fresh heart but required a higher atrial pressure and greater presystolic ventricular distention The corollary follows that at controlled heart rates the competence of the myocardium may be tested *by comparing the systolic discharge at equivalent venous pressures or by determining the venous pressure required to produce equivalent stroke volumes* This procedure has been used by Krayer[16] in the heart lung preparation and by the author[19] in the intact animal

5 In some experiments in which simultaneous volume and pressure curves from the ventricles were recorded it appeared that considerable increase in presystolic ventricular size took place while the presystolic or initial tension in the left ventricle remained unchanged or actually fell (Patterson Piper and Starling[11]) However at the time these investigators worked it was not realized that slight shifts in the entire pressure curve cannot be excluded unless a base line for optical pressure curves is simultaneously recorded From their observations the inference seemed warranted that the presystolic size (stretch) of the ventricles is not determined solely by actual filling pressures (mean atrial pressures) but is affected also by inherent variations in their rate of relaxation and elastic or tonic resistance to stretching On the whole they believed that the mammalian ventricle unlike that of the frog studied by Frank rarely reaches a state of static relaxation before the succeeding beat supervenes

From these observations Starling s oft quoted law of the heart was derived[20] There is a general impression that the graphic representation of the law often reproduced was based on data from these experiments The careful reader will discover the frank statement that the published curves are reproductions of graphs previously published by Blix and by O Frank (Patterson Piper and Starling[11])

So far our analysis of the mechanical condition of the heart s contraction does not differ essentially from Frank s classical exposition of the mechanical events affecting contraction of the frog s heart In this work however Frank was dealing with contractile tissue which had long periods of diastole so that it had reached a static condition before the beginning of systole and he found that the energy set free in the excited condition (as measured by the tension set up) was proportional to the initial i e diastolic tension on the muscle But in this case it is not easy to decide whether the determining factor is really the initial tension or the initial length of the muscle fibres

In the mammalian heart we are dealing with an organ which is contract

ing rapidly and rhythmically such contraction being a necessary condition for the preservation of its functional activity The condition of the heart therefore as to both tension and length of its muscle fibres is altering continuously during diastole from one beat to the next

In Frank s experiments on the frog s heart the initial length was proportional to the initial tension so that the augmentation of energy set free on contraction might have been due either to the increased tension or to the increased length In our experiments we have found that it is length rather than tension which determines the energy of contraction

We thus find no constant connection between the diastolic tension and the succeeding contraction though as a rule the two quantities will be altered together But we do find a direct proportion between the diastolic volume of the heart (i e the length of its muscle fibres) and the energy set free in the following systole

The law of the heart is therefore the same as that of skeletal muscle namely that the mechanical energy set free on passage from the resting to the contracted state depends on the area of chemically active surfaces, i e on the length of the muscle fibres *This simple formula serves to explain the whole behaviour of the isolated mammalian heart—its movement powers of adaptation to varying demands made upon it its behaviour to fatigue and the influence of its nerves or chemical agencies such as acid ions or adrenalin* (Author s italics)

The basic idea underlying Starling s law of the heart namely that myocardial response is determined basically by the degree to which fibers are stretched has been supported with one exception [21] by all subsequent investigators [22-31] However attention may be directed to the fact that all investigators have assumed the existence of a linear relation between presystolic ventricular capacity and length of fibers and between presystolic intracardiac pressure and initial tension on muscle fibers The validity of this assumption for the mammalian ventricles composed of complicated superimposed muscle bands arranged to pull in different directions has never been adequately established

In 1922 Wiggers and Katz[3] restudied the mechanism of adaptation *to increasing venous return by means of cardiometric technic* in a controlled circulation preparation The preparation, as progressively improved in subsequent researches is diagrammatized in figure 13 The heart of a lightly anesthetized dog is exposed under artificial respiration just enough for the animal to retain natural diaphragmatic

movements This offers a simple indication that blood gases remain essentially normal The cardiac nerves are severed The heart rate is controllable within wide ranges it is reduced to 40 or 50 per minute by clamping the sinus node and then driving the heart by electric shocks applied to the right atrium Venous return can be decreased through graded compression of the inferior vena cava or increased by an infusion of warm saline into a jugular vein The reduction in blood viscosity which accompanies such infusion is advantageous dynamic-

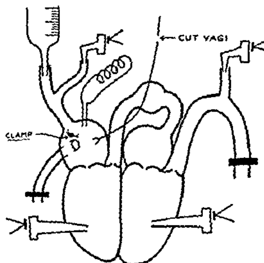


Fig 13 —Diagram illustrating the controlled circulation preparation for studying separate determinants of ventricular response Discussion in text

ally for it has proved just about sufficient to maintain a constant diastolic pressure despite increasing stroke volumes Arterial resistance can be controlled by tightening or loosening an adjustable clamp placed around the lowest portion of the thoracic aorta

Volume curves of the ventricle are recorded optically together with arterial pressure pulses as described elsewhere [3, 12] Typical curves are shown in figure 14 The volume tracings descend with diminution of ventricular volume during systole and rise during diastolic filling Changes in slope (1–9) indicate changes in the rate of ventricular

emptying and filling During the phase of isometric contraction (2-3) the curves either rise or fall slightly These variations are unavoidable artefacts created by slight shift of the cardiac base with respect to the rubber diaphragm During systolic ejection (3-7) several changes in rate of emptying corresponding to inflections of the aortic pressure curve are indicated by vertical lines The rapid ejection rate from 3-6 and the marked reduction from 6-7 are particularly noteworthy Systole ceases at 7 and the interval 7-8 demarcates the isometric

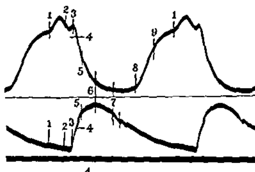


Fig 14 —Simultaneously recorded volume curve of ventricles (upper) and aortic pressure (lower) showing corresponding inflections during phases of ejection and division of systole and diastole into commonly accepted phases (1 2) atrial systole (2-3) isometric contraction (3 5) period of maximal systolic ejection (5-7) period of reduced systolic ejection (7) end of systole (7-8) isometric relaxation (8-9) rapid diastolic filling (9-1) retarded diastolic inflow (diastasis) (After C J Wiggers Physiology in Health and Disease courtesy of Lea and Febiger Philadelphia)

relaxation phase of the ventricles Ventricular filling occurs rapidly at first (8-9) and then more gradually (9-1) dividing the filling into phases of rapid inflow and diastasis This is followed by atrial systole (1-2)

The results obtained by Katz and myself[3] in the main confirmed those of Starling and his group but some amplification and certain differences were found

1 During the compensatory stage of increased venous return (compare curves A and B in fig 15) ventricular filling proceeded more rapidly throughout diastole that is during the successive periods of rapid inflow diastasis, and atrial contraction The larger systolic

discharge was accomplished by a greater velocity of ejection a prolongation of the ejection period (compare a and b) and occasionally even more complete emptying It is obvious at a glance that such curves are not superimposable as regards either their systolic or diastolic limbs Optical pressure curves from the right ventricle (lower series fig 15) demonstrated that the presystolic intraventricular

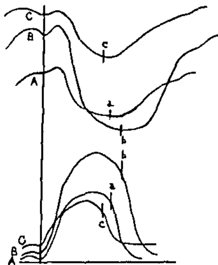


Fig 15 —Changes in configuration of ventricular volume curves (upper series) and right ventricular pressure pulses (lower series) during progressive increase in rate of venous return All curves matched at beginning of ventricular systole a b c denote ends of systole and illustrate changes in relative durations of systoles (A) control (B) during compensatory stage (C) during decompensatory stage (After C J Wiggers Physiology in Health and Disease courtesy of Lea and Febiger Philadelphia)

pressure (initial tension) increased steadily the gradient of pressure before ejection (isometric phase) was steeper and the curves reached higher peaks The larger volumes ejected by the right ventricle under higher pressure necessarily caused an elevation of left atrial pressure Contrary to Starling s observations, Opdyke and his associates[33] have recently demonstrated that the increase in pressure was much larger in the left than in the right atrium owing to a lesser distensibility of the left atrium and its tributary veins

2 Contrary to interpretations by Starling and his associates we found that reduction in stroke volume with excessive rates of venous inflow was not conditioned by the fact that the ventricles had reached their distention limits decompensation developed while the process of diastolic distention was actually accelerating (fig 15 B C) In other words it appears that beyond a critical degree of stretch additional extension either has a reversed effect on the release of mechanical energy or contraction is hindered by the greatly increasing diastolic tension This also accords with O Frank s observations on frog hearts[8] and with those of Lundin[34] on stretched moieties of ventricular muscle Analysis of volume and right ventricular pressure curves (fig 15 C) indicated that despite a large increase in diastolic size and in initial tension the mechanism of discharge changed the ventricles emptied themselves less forcibly and completely indeed the systolic size was sometimes smaller than the normal diastolic size An enormous increase in residual volume was apparent (see a and c curves A and C) indicating that a considerable effective volume of blood stagnated in the heart during progressive decompensation The systolic pressures in the right ventricle and pulmonary artery decreased and consonant with Starling s results pressure in the left atrium fell

3 With constant venous return and right atrial pressures the cardiac output was found to be far from constant at different heart rates as the British investigators claimed Under carefully controlled atrial pressure the alterations in stroke volume with progressive acceleration followed the predictions of Y Henderson rather better than the experimental results of Starling and his group However unless arterial and venous pressures were readjusted with every change in heart rate the beats were not superimposable and accurate predictions as to the relation of cardiac output to heart rate could not be made

The reasons for the variable effects of heart rate changes on stroke volume and cardiac output per minute have gradually become clearer from the study of a large number of ventricular volume curves The integration of a large number of physical and physiologic determinant on ventricular filling are involved An attempt is made to dissociate the chain of events with the aid of the diagram in figure 16 The heavy curve (N) represents a ventricular volume curve under normal conditions at a heart rate of 75 per minute The record is taken in such a manner that ventricular emptying is indicated by the downstroke

and filling by the upstroke The residual volume is indicated without ordinate values The phases of systole and diastole for this beat are numbered as in figure 14

An acceleration of the heart approximately to 120 per minute would according to Y Henderson s scheme merely cut into the filling curve as indicated by the arc A This however is an oversimplification of

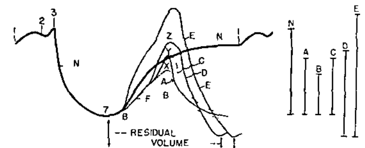


Fig 16 —Heavy curve (N) typical volume curve for heart cycle 0 8 second (75 per minute) Numerals same as in figure 14 Assembly of superimposed ventricular volume curves illustrate variable factors that may influence stroke volume when heart rate increases to 120 per minute (A) Abridgement of natural filling and reduction of stroke volume according to Henderson (B) Further reduction in systolic discharge owing to coincident reduction in atrial pressure and reduced filling rate shown at F and diminished force of atrial systole at X (C) Restoration of stroke volume to control of curve A by greater effectiveness of an atrial systole (Y) which supervenes immediately after or during rapid inflow (D) Increase in stroke volume to that of a beat with long cycle (N) as a result of accelerator nerve action or adrenergic humoral effects which increase force of atrial contraction Z and more completely empty the ventricles (reduction of residual volume) (E) Further augmentation of systolic discharge through simultaneous increase in venous return and more rapid filling as in exercise Lines on right (N E) indicate at a glance comparative stroke volumes for corresponding volume curves

changes that actually take place In the first place despite constancy in returning blood volumes such acceleration very quickly reduces the pressure and volume of blood in the atria in a mechanical way Simply stated more blood is pumped per minute than is received As a result the rate of filling during the rapid inflow phase tends to become more gradual as in the curve labeled F Since the atria start their contractions at a shorter initial length the vigor of their contrac

tions would be diminished and it might be expected that their contribution to ventricular filling would be reduced as indicated in the wave X However this diminishing effect of atrial contraction appears to be offset by the fact that atrial contractions coming at the time of incomplete ventricular filling are more effective than those that occur after a long diastasis as in the solid line curve As a result the increment becomes somewhat greater as indicated in the wave Y which may restore the systolic stroke C approximately to that of stroke A Necessarily the diastolic filling curves are not superimposable but the net effect on stroke volume approximates Henderson s predictions If in addition the increase in heart rate is induced by activation of the accelerator mechanism and release of the vagus mechanism the force of atrial systole may be increased significantly and the contribution to ventricular filling may be represented by wave Z Under such hypothetic conditions the stroke volume D may almost equal that of the control beat A for the accelerator mechanism also acts directly on the ventricles to reduce their residual volumes

Such an approximate proportionality of cardiac output to heart rate can obviously be maintained only as long as the volume of venous return equals the cardiac output If as a result of many conditions—hemorrhage and shock for example—this is not accomplished these compensatory reactions cannot be maintained If on the other hand venous return augments at the same time that the heart accelerates as in exercise the stroke volumes can definitely exceed the normal as illustrated in curve E This analysis of the many coefficients which affect ventricular filling explains why investigators have differed (a) as to the contribution of atrial systole to ventricular filling and (b) as to the effect of heart rate changes on cardiac output per minute

It seems apparent now that the constant cardiac outputs obtained by Starling and his associates over wide ranges of heart rates were due to a fortuitous balance between these variable factors The British investigators failed to recognize that the available supply and pressure of blood in the right atrium is determined as much by changes in cycle length as by the pressure head in a venous reservoir Furthermore as Krayer[18] has pointed out these investigators altered heart rate through changes of temperature of the inflowing blood which is

certainly not without influence on the inherent contractility of the ventricles

Intrinsic Cardiac Factors

Our analysis of the relationship between atrial volumes and pressures duration of the inflow periods and force of atrial contractions on the one hand and systolic discharge and cardiac output per minute on the other accord basically with the law of initial length The resultant effect of filling pressure, atrial activity and the available filling time regulate the degree of ventricular distention (initial length) realized at any given cycle length and this in turn determines the velocity volume and duration of the systolic discharges However this is only a first approximation to reactions of the heart muscle at a given initial length in the body As Starling and his group pointed out at equivalent initial lengths a heart in good condition responds with a larger stroke volume than a fatigued heart Also as Wiggers and Katz[3] pointed out the pattern of ventricular emptying is not solely governed by presystolic filling but it is also affected by reduction in coronary flow

Hearts stimulated or depressed by drugs chemical changes in the blood or through nerve actions show similar variations In a study of *the dynamics of drug actions I pointed out in 1927*[3] *that the vigor* and pattern of ventricular contraction and consequently its systolic discharge can be influenced (a) by agents which primarily affect the *contractility of the myocardium as well as (b) by those which sec*ondarily affect contractility through changes in initial tension or length such as are induced by alterations in venous return arterial resistance and heart rate To the latter may be added hydrodynamic effects produced by such pathologic conditions as coronary insufficiency valvular lesions anomalous cardiovascular circuits pulmonary vascular changes and pericardial effusions In short the ventricles do not obey the law of all or nothing at any given degree of fiber stretch their magnitude of response depends on the physiologic state of myocardial reactivity Starling was certainly aware of the importance of the condition of the heart muscle but did not include this in phrasing the law of the heart

I would suggest therefore that to avoid ambiguity or misin

terpretation the law of the heart be amended somewhat as follows

The law of the heart is thus the same as the law of muscular tissue generally that the energy of contraction however measured is a function of the length of the muscle fiber *under equivalent states of responsiveness* Within recent years the operation of the law of initial length has seriously been questioned on the basis of studies of the human heart by catheterization technics [36] We may predict with confidence that when we are able to overcome the technical difficulties that still impair the accuracy of pressure determinations in catheterization studies [37] a careful evaluation of results will demonstrate the validity of the law of cardiac performance However I predict that complete assessment of the regulation of cardiac performance is not likely to succeed from analyses of hemodynamic data during health and disease alone because innumerable variables are bound to be concerned The multiple factors which can separately influence the response of the myocardium at equivalent initial lengths must be submitted to intensive experimental studies of a basic sort A wide new field awaits exploration Nothing would give me greater pleasure than to attack the many facets of this interesting problem However since I am approaching the end of my experimental career I can perhaps best serve the cause of cardiac research in exhorting a new generation of investigators to accept the challenge of their execution

Summary

Three classic discoveries—by Bowditch in 1869 by Howell and Donaldson in 1884 and by O Frank in 1895—laid the foundation for the basic laws which govern the regulation of ventricular responses Years of further experimentation have not only shown that the mammalian heart operates according to these basic laws but have also elucidated the many variables which sometimes obscure the evidence that these basic laws are important under normal and pathologic conditions

In 1906 Y Henderson evolved a law of uniformity of cardiac behavior which offered a geometric plan for roughly evaluating the relation of ventricular filling at different cycle lengths to systolic discharge and cardiac output but his conclusion that the systolic discharge at any given heart rate cannot be increased above its normal value has not been supported by further studies

In 1914 Straub and the writer independently reported experiments

on mammalian hearts which appeared to show that the reactions of the mammalian ventricles to changes in venous return and arterial resistance harmonized with laws derived by Frank from studies on frogs hearts These experiments like those of O Frank were unable to determine whether changes in presystolic pressure (initial tension) or volume (initial length) fundamentally regulate the degree of responsiveness however measured Shortly after the publication of these researches Starling and his associates on the basis of experiments on the heart lung preparation which were highly suggestive but not quite conclusive concluded that in the reaction of the heart to increased inflow and increased resistance the only factor which constantly varies with the response of the ventricles is the volume of the heart that is the length of its muscle fibers The law of the heart was thus reduced to the formula that the mechanical energy set free on passage from the resting to the constricted state depends on the area of chemically active surfaces i e on the length of the muscle fibers This basic concept has subsequently been validated by nearly all investigators

In 1922 the writer and Katz delineated the detailed changes in the patterns of ventricular filling and emptying occasioned by alterations in venous return arterial resistance and heart rate and analyzed their relation to presystolic ventricular volume It was concluded that Starling s interpretations required some modification For instance the rate and degree of ventricular filling are a resultant of the atrio ventricular pressure gradient the variable effect of atrial systole and the time interval available for ventricular filling Furthermore these and subsequent studies by the writer have revealed that while the mode duration and extent of ventricular emptying are in a measure determined by the presystolic size primary factors which affect the responsiveness of the myocardium are likewise of great importance These include such factors as coronary blood supply humoral agents and nervous actions on the ventricular muscle

It is suggested that the operation of the law of initial length will also be found valid in the human heart under equivalent states of myocardial responsiveness

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CHAPTER III

Dynamics of Ventricular Contraction under Abnormal Conditions*

WITHIN the past two decades clinical and experimental studies of cardiac output—per minute and per beat—have yielded much important information concerning the nature of cardiovascular disorders. However, a basic understanding of such conditions also requires a comprehension of the ways and means by which cardiac output is either maintained or altered. The dynamics of ventricular contraction, *which concerns itself with the mechanisms through which cardiac output is altered*, can be evaluated to a considerable extent by a rigid analysis of pressure pulses recorded from the ventricular cavities.

Now it happens that during various periods since 1912 I have used such pressure pulses to study the basic changes in cardiac behavior produced during abnormal circulatory conditions in experimental animals. Since this work was published largely in journals of physiology previous to the awakening of clinical interest in cardiodynamics, much of it probably lies dormant on library shelves. In view of the current clinical interest, the time seems appropriate for recalling some of these studies and suggesting that experimental work of this nature be given consideration in the evaluation of human cardiovascular problems. It remains my considered judgment that deductions regarding cardiac behavior derived from controllable acute experiments on the dog's heart can be transferred to human hearts provided that proper reserve and caution are exercised.

The Interpretation of Ventricular Pressure Pulses

An investigator who attempts to draw conclusions from records of ventricular pressure pulses must exercise certain precautions if he

*The Henry Jackson Memorial Lecture delivered before the Massachusetts Heart Association Inc, Boston, Mass, June 4, 1951

wishes to avoid the formulation of wrong deductions Recorded curves should always be examined and evaluated as to their reliability that is to say, whether they truly depict pressure fluctuations or are distorted by artefacts of registration The latter are more easily introduced than avoided Distortion of ventricular pressure curves results from the use of inadequate manometer systems [1, 2] Theoretic physical formulations and practical tests have demonstrated that reliable curves can be recorded only by a manometer system which has an adequate frequency and proper damping characteristics expressed

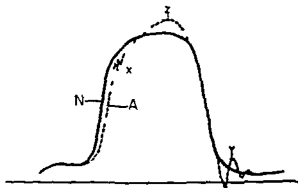


FIG 17 —Two graphs of a true left ventricular pressure pulse (N) and the same deformed through artefacts (A) In the latter the delayed rise the superimposed vibrations (X) the dip and aftervibrations (Y) following relaxation are artefacts common to undamped low frequency systems The late systolic rise (Z) which can generally be abolished by changing position of intracardiac sound is probably produced by location of sounds in pockets

by the logarithmic decrement of its free vibrations There have been and still are investigators who maintain that curves with high frequency components can be inscribed with properly damped low frequency manometers Such a task appears to resemble one which would require a bass fiddle player to perform a musical score written for flute or piccolo

Artefacts are also produced through periodic obstruction of manometer tubes or through displacement of a catheter and the heart in relation to one another during contraction and relaxation but these are usually recognizable and when present must be discounted A few common distortions of ventricular pressure curves are shown in

the assembly of records in figure 17 The heavy curve (N) represents the actual pressure fluctuations the other curve (A) combines various distortions which may appear singly or in combination in records Curves recorded by manometers of low frequency are characterized by retardation of the pressure rise (curve A) the production of vibrations at the onset of ejection (x) and a negative dip and/or after vibration shown at y Location of a trocar or sound in intraventric

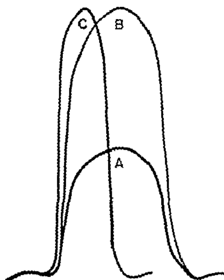


FIG 18 —Identical ventricular pressure pulses recorded with manometers of different sensitivity (A B) and on paper traveling at different speeds (B C)

ular pockets e g behind papillary muscles or valves probably gives rise to curves with a secondary peak at the end of systole as shown at z

Ventricular pressure curves may display apparent rather than real differences in their patterns depending on the sensitivity of the manometers employed and the speed at which curves are recorded on moving paper Thus curve A in figure 18 is a typical normal curve If the same pressure pulse is recorded by a manometer having twice the

sensitivity curve B emerges and if this record be taken at half the paper speed curve C develops It is apparent that important inflections tend to be obscured in curve C and that artefacts might not be recognizable If in addition the amplitude of such a curve is reduced to 1 0 cm by use of direct recorders contour changes cannot be inferred A judicious balance between ordinate and abscissal values is obviously important in the registration of pressure pulses

Successive Myocardial and Dynamic Events during the Cardiac Cycle

A proper interpretation of myocardial activity through analysis of the ventricular pressure pulse requires a knowledge of its relationship to other cardiodynamic events The relation of ventricular pressure variations during successive phases of the heart cycle to pressure changes in the aorta and left atrium to a surface myogram to acoustic phenomena to volume changes of the ventricles and to an electrocardiogram (standard lead II) are shown in figure 19 The persistence with which curves of inaccurate contours and erroneous time relations continue to appear in papers and textbooks makes publication of such a chart desirable A comprehension of correlated events expressed in such a series of curves was once regarded as an academic exercise in the current era of hemodynamic studies it becomes an inescapable requirement

The subdivision of the cardiac cycle which I suggested[3] in 1921 has apparently gained rather general acceptance According to this scheme systole begins with the rise of ventricular pressure at A and ends with the release of tension in all muscle units at F (fig 19) It is divided into phases of *isometric contraction* (A–C) *maximum ejection* (C D) and *reduced ejection* (D–F) The subsequent period of diastole is divided into phases of *protodiastole* representing the time required for closure of the *semilunar valves* (F–G) *isometric relaxation* (G–H) *rapid ventricular filling* (H–I) *diastasis* (I–J) and filling by *atrial contraction* (J–K)

Abnormal patterns of ventricular contraction cannot be inferred from ventricular pressure pulses unless an investigator or reader possesses the capacity for translating the tracings into mental pictures of processes which take place in the heart and vascular system during the period of the heart cycle outlined by the ventricular pressure curve We may therefore review briefly the main muscular and

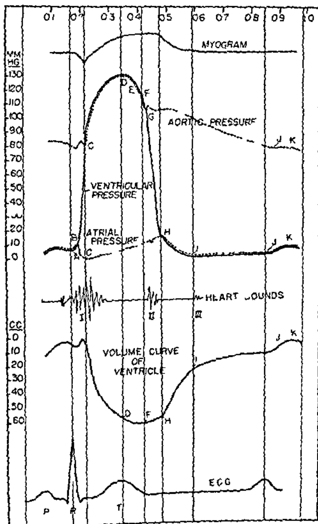


Fig 19 —Chart showing correlation of various dynamic mechanical acoustic and electrical events during a cardiac cycle

hemodynamic events which are associated with the phases of isometric contraction systolic ejection and isometric relaxation As a prelude to such discussion the dynamic effort of the heart during

the respective phases may be compared to the task of (1) raising a pail of water from the ground to a high level (2) holding it at this level while most of its contents are thrown with some force over a wall and (3) bringing the pail back to the ground for refilling

At the onset of mechanical systole at A the entire myocardium of *the left ventricle has been excited This is evidenced by its coincidence* with the peak of R of a standard or direct electrocardiographic lead[4, 5] Owing to a latency however, only the initially excited fractions have started to contract As more and more contractile fractions summate the pressure rises slowly at first (A–B) but very rapidly as soon as all fractions participate in the summation process (B–C) Since the mitral and semilunar valves are closed during the interval A–C and blood neither enters nor leaves the left ventricle contraction is essentially isometric that is energy of contraction is converted to tension Actually however a little energy is lost through a slight yielding of the valvular structures and in readjustments in the form *and position of the heart In the development of a rigid muscular state* the ventricles rotate assume a more globular shape and exert a traction on the atria and large vessels Myograms recorded from the left ventricular surface such as are reproduced in figure 19 reveal that the surface layers may even lengthen as a result of changes in form of the ventricle However reduction in the base to apex axis demonstrates that the septal fibers undergo a shortening This afterloaded mode of ventricular contraction has the advantage that sufficient vis a tergo is developed to start quickly and continue a brusque and forceful ejection of blood into the aorta against a relatively high aortic resistance

The ejection of blood takes place within a relatively short period (C–F) it is about 0 25 second in man and less in lower animals Reference to volume curves of the ventricles (fig 19) reveals that two thirds of the whole stroke volume is ejected during the first half of this period (C–D) and a comparatively small fraction during the latter half (D–F) Since efflux of blood from aortic branches exceeds uptake from the ventricles during the latter half of ejection the pressures in the aorta and left ventricle decline (D–F) Thus the summits of the ventricular and aortic pressures demarcate the transition from rapid to reduced systolic ejection More than this, the inflections of the ventricular as well as of the aortic pressure curves from C to F

reflect minor changes in the rate of systolic ejection This is clearly illustrated by comparing changes in ventricular volume with pressure variations in the root of the aorta in figure 20 The initial steep rise of aortic pressure (3–4) is accompanied by a brusque movement of only a small volume of blood into the aorta The continued elevation of *aortic pressure from 4 to 5 is attended by a rapid emptying of the* ventricle During the slower rise of aortic pressure to a summit (5–6) the rate of ventricular emptying diminishes progressively and during the systolic decline of pressure (6–7) it is very low It is apparent that

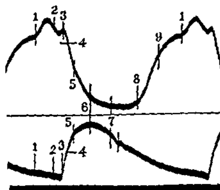


FIG 20 – Simultaneous records of changes in a normal ventricular volume (upper) and aortic pressure (lower) demonstrating the correspondence of inflections (1–7) during systolic ejection Volume curve is inscribed so that emptying of ventricles is recorded as downstroke filling as upstroke (After C J Wiggers Physiology in Health and Disease courtesy Lea and Febiger Philadelphia)

despite the variable efflux from the aorta the configuration of the aortic (and ventricular) pressure pulses is dominated by the changing rates of ventricular emptying

From a dynamic standpoint mechanical systole terminates at F (fig 19) for all muscle fractions have ceased to develop tension[3] The completion of the T deflection by this time indicates that repolarization has been completed[4] However theoretic considerations[6] and the responses to electrical stimuli[7] strongly favor the view that muscle fibers have ceased to develop tension earlier for example at F This does not mean that a lengthening of myocardial fibers has com

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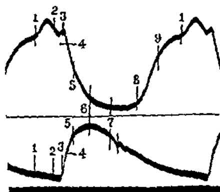


Fig. 20. Simultaneous records of changes in a normal ventricular volume (upper) and aortic pressure (lower) demonstrating the correspondence of inflections (1–4) during systolic ejection. Volume curve is inscribed so that emptying of ventricles is recorded as downstroke, filling as upstroke. (After C. J. Wiggers: Physiology in Health and Disease, courtesy Lea and Febiger, Philadelphia.)

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menced On the contrary myograms reproduced in figures 19 and 21 demonstrate that the ventricular relaxation starts with a reduction of tension for 08 second or longer (G–H) before the fibers lengthen (H–I) and ventricular filling begins[8] It has been tempting to relate the gradient of pressure decline and the duration of the isometric relaxation phases (G–H) to physiologic differences in the relaxation process However the effects of physical forces cannot be wholly excluded These include (1) the refilling of coronary vessels (2) the volume of residual blood remaining after ejection (3) the pressure

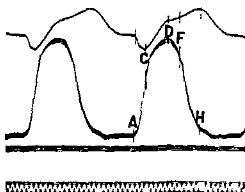


Fig 21 —Simultaneous records of the changes in length of a small area of the left ventricular surface (upper curve) related to a ventricular pressure pulse (lower curve) A C isometric contraction C D maximal systolic ejection D F reduced ejection and protodiastole F H isometric relaxation Note that shortening of surface fibers begins at C and terminates at H Time 0 second

at the onset of isometric relaxation and (4) the atrial pressure which determines the time at which curves intercept at H It may be added however that myograms such as are reproduced in figure 21 offer no support for the view that refilling of the coronary vessels during isometric relaxation stretches the myocardium

Determinants of Myocardial Responses

The contraction pattern of the ventricles is determined by factors that affect the physiologic condition of the heart muscle directly and by those that act through changes in input and output loads The

former have been termed primary and the latter secondary coefficient (see Chapter II) Primary coefficients[9] include the direct myocardial effects of local metabolites fatigue abnormal chemical constituents of the blood including drugs coronary insufficiency and nervous impulses Through these true cardiac stimulation or depression is produced Secondary coefficients[9] cause alterations in cardiac output by modifying the diastolic filling or arterial resistance In pathologic conditions tertiary coefficients can significantly modify the ventricular contraction patterns in mechanical ways These include such factors as an abnormal sequence or deletion of fractionate contractions and valvular lesions which cause the ventricles to contract in a loaded or isometric rather than an afterloaded manner

As Starling and his associates[10] inferred from studies on a heart lung preparation the responses of a ventricle under many normal and pathologic conditions are determined by its presystolic size or the initial length from which fibers start their contraction Personal experience has confirmed Frank s earlier postulate that with exceptions to be noted later changes in initial length are produced by alterations in ventricular pressure at the onset of contraction namely by the initial ten ion Such changes though small are usually discernible in optical records of sufficient amplitude However controlled conditions are required for studying the effects of such a secondary coefficient These conditions are that the heart rate remains constant and that the myocardial reactions are not simultaneously affected by primary or tertiary factors enumerated above

In Chapter II experimental procedures were described by which heart rate can be kept constant in the intact circulation while venous inflow and arterial resistance are independently adjustable (see fig 13 p 41) Basic studies on such controlled circulation preparation have revealed that alterations in the pattern of ventricular contractions produced by primary and secondary coefficients can be distinguished by the relation that the amplitude form and duration of contractions bear to initial tension Thus as illustrated by curves 1 and 2 of figure *22I* progressive elevations of initial ten ion at A are accompanied by increasing force and duration of contractions up to a critical level After the critical degree of stretch has been exceeded initial tension increases more rapidly and is followed by contractions having a more gradual ri e a lower amplitude and a shorter duration

as depicted in curve 3 of figure 22*I* These changes from a normal curve N illustrate compensation and decompensation with increasing input loads It may be added that the decompensatory responses must probably be assigned to some innate effect on the myocardium,

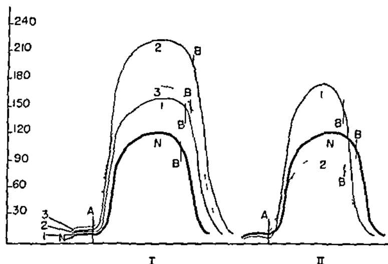


Fig 22 —Assemblies of transcribed ventricular pressure pulses comparing the effect of progressive increase in initial length and tension (secondary coefficients) and the effects of primary myocardial coefficients

I N normal curve 1 2 compensatory responses to increasing initial tension following rapid saline infusion 3 decompensating response from over distention by a large infusion Note progressive increase in initial tension at A and lengthening of systole A B

II N normal curve 1 augmentation of contraction with fall in initial tension (A) and shortening of systole (A B) following a dose of epinephrine in a preparation with controlled heart rate 2 depression of contraction with elevation of initial tension slower gradient and abbreviation of contraction (A B) following a small dose of chloral hydrate heart rate controlled

perhaps a fatigue process The effects of primary coefficients are illustrated by the curves of figure 22*II* If the myocardium is stimulated as by epinephrine or accelerator nervous impulses while heart rate and venous return are kept constant the contractions become larger steeper and shorter in duration the stroke volume increases and consequently the initial tension declines Such a response is shown

in curve 1 If on the contrary the ventricular muscle is depressed as by chloral hydrate or Pitressin the ventricular contractions become more gradual reach a lower summit and are abbreviated the stroke volume is reduced and initial tension is elevated through development of a larger reserve volume

From these observations the rule can be deduced (1) that secondary changes in ventricular response can be inferred from ventricular pressure curves when initial tension and amplitude of contraction alter in the same direction and (2) that primary changes in ventricular response are characterized by opposite changes in initial tension and amplitude of contraction It must be recognized of course that in the body primary and secondary factors frequently operate at the same time Thus even when tertiary factors are not involved it often becomes difficult if not impossible to determine the basic mechanisms which govern ventricular performance As was emphasized in Chapter II such a dilemma arises when comparative observations are made at differing heart rates for the duration of diastolic filling affects initial tension and length and therefore the magnitude vigor and duration of ventricular contractions The advantages of studying the mechanism of abnormal cardiac responses in experimental animals in which heart rate as well as input and output loads are controllable rather than in human subjects in whom this cannot be achieved should be obvious

With this brief orientation we shall proceed to analyze the mechanisms which determine ventricular contraction patterns in a number of experimental conditions which simulate clinical circulatory disorders

Pericardial Effusion

The dynamic changes produced by degrees of pericardial effusion which significantly interfere with ventricular filling and thereby cause reduction in cardiac output have been thoroughly worked out by a number of investigators[18-19] Our discussion is advisedly limited to a consideration of the support that studies on pericardial effusion have given to the thesis that change in initial length rather than initial tension is the basic secondary determinant of ventricular response

Since initial tension and length generally alter in the same direction it has proved difficult to draw inferences as to which of the variables

basically affects myocardial response. The deduction of Starling and his associates[10] that the energy of contraction however measured is determined by changes in initial length of the muscle fibers has been since confirmed by numerous studies in which a dissociation of initial

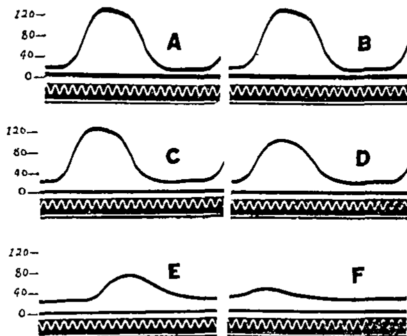


Fig. 23.—Series of left ventricular pressure curves showing how progressive increases in pericardial fluid and pressure steadily elevate initial tension in relation to a base line but decrease maximal ventricular pressures and gradients of contraction. Pericardial pressures expressed in mm. Hg as follows: Curve A = 15 mm.; B = 75 mm.; C = 90 mm.; D = 100 mm.; E = 135 mm.; F, very high, reading doubtful.

length and tension was achieved by experimental expedients. (For bibliography see refs. 22–31, page 51.)

When the volume of liquid within the pericardium exceeds the natural available space the intrapericardial structures are compressed by increasing pressure around them.[11] The initial tension within the ventricles rises almost proportionally with intrapericardial pressure but their diastolic size decreases owing to the impairment of filling

The fact that changes in initial tension and length are dissociated thus afforded an opportunity to determine experimentally which of these factors dominates cardiac response.[15] Some of the changes found in ventricular pressure pulses are illustrated by records of figure 23. Each increase in pericardial and initial ventricular tension is accompanied by development of less pressure and slower gradients. The durations of isometric contraction and ejection decrease despite some lengthening of the heart cycle. All of these reactions are obviously the opposite of those normally associated with increase in initial tension, whereas they accord with changes resulting from reduction in presystolic size or initial length of myocardial fibers.

Hypervolemia

The basic reactions which accompany an increase in plasma volume can be reduplicated experimentally by venous infusions of saline solutions or plasma. Briefly recapitulated, the following chain of events takes place: the greater output of the right ventricle not only elevates left atrial pressure at the moment when the mitral valves open but also induces more vigorous atrial systoles. Through these two mechanisms the left ventricle is more completely filled and initial tension is elevated. The ventricular responses are those exemplified by curves I and II of figure 22. Characteristic effects consist of a steeper isometric gradient, quicker rise of pressure to a higher peak during ejection, and a prolongation of systole. The larger stroke volume which accompanies these pressure changes is achieved through the combined effects of a higher velocity of ejection and prolongation of the ejection phase.[16]

Acute production of polycythemic hypervolemia evokes similar responses. Figure 24 shows representative curves recorded by Gregg and myself[17] after injection of sedimented matched corpuscles over a period of five minutes. Comparison of curves A and B reveals an elevation of initial tension, a steeper isometric gradient, a higher systolic pressure, and an extension of systole. All are typical changes induced by concordant increases in initial tension and length. The effects persist for a considerable time, as shown in curves C and D recorded respectively 80 and 115 minutes after the infusion of erythrocytes had ceased. An analysis of aortic pressure pulses led to the conclusion that the augmented peripheral resistance occasioned by

greater viscosity of the blood and the strain of a higher input load were less important determinants of left ventricular response However

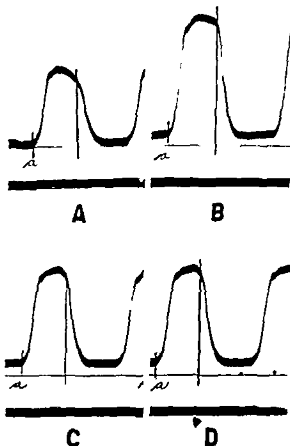


Fig 24 —Four left ventricular pressure curves A control B shortly after *infusion of 700 cc sedimented matched corpuscles in 5 minutes C 80 minutes* later D 115 minutes later Observe elevation of initial tension at a and higher pressure maxima Durations of systole as follows in seconds A 0 172 B 0 185 C 0 1 0 D 0 172

ever it may be noted in these records that whereas systole is somewhat prolonged in curve B it shortens again in curves C and D suggesting an influence of the higher output load (see later)

The recently reported observations from Gregg's laboratory[17] that following blood transfusion no consistent relationship was found between stroke volume and presystolic pressure in the left ventricle do not necessarily negate the preceding conclusion. They could equally well be interpreted as evidence for the limitations of the dye dilution method employed.

Oligemia

Reduction in blood volume such as exists after a severe hemorrhage has reversed effects on ventricular pressure curves. However, if a state of hypotension is maintained for long intervals, the myocardium

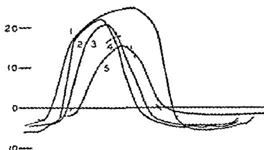


FIG. 25.—Assemblage of transcribed curves showing pressure changes in the right ventricle after hemorrhage and transfusion. Discussion in text. (After Opdyke and Wiggers.)

is depressed presumably through defective coronary flow. As a result the ventricles expel smaller stroke volumes, their residual volume becomes larger, and initial tension returns to normal levels.

Since pressure and resistance decline less in the pulmonary artery than in the aorta, the basic effects of prolonged diminution in venous return are exhibited better in the right heart. Some changes in right ventricular behavior reported by Opdyke and myself[18] are reproduced in figure 25. Curve 1 represents a right ventricular pressure curve taken as a control. Curve 2 was recorded shortly after arterial mean pressure had been reduced to 65 mm. Hg by a severe hemorrhage. The isometric ascent remains steep despite a fall in initial tension, but systole is typically abridged and the systolic summit is lower. Curve 3 was recorded after a state of hypotension at a 50 mm. Hg

level had persisted for 88 minutes The slower rise of pressure to a lower summit and a further abbreviation of systole regardless of the slight recovery of initial tension are obvious Curve 4 was recorded immediately after a further reduction of arterial pressure to 30 mm Hg and curve 5 45 minutes later Initial tension is elevated above that of the control curve 1 but the gradients and summits of the pressure curves are decidedly reduced Such deterioration of contraction with rising initial tension strongly suggests that a primary myocardial depression has supervened (For further discussion see reference 2)

Arterial Hypertension of Peripheral Origin

The effects of increased peripheral resistance on ventricular contraction patterns can be analyzed best by applying a mechanical constrictor to the aorta just above the diaphragm[1, 19] Even so adaptation occurs in two stages The first stage illustrated by curves labeled 2 and 4 figure 26 persists only for the first two to five beats after a sudden constriction The changes in the ventricular pressure pulses are solely attributable to increased aortic resistance for the initial tension remains unaltered Since ventricular pressure must be elevated to higher levels before the semilunar valves open isometric contraction (A–C) is slightly prolonged The isometric pressure gradient is not affected because the ventricle is not exposed to the higher aortic pressure during this period

In response to a higher aortic pressure the systolic ejection period (C–F) is typically abridged[16] and to such an extent that systole as a whole (A–F) is also shorter The pressure rises to a higher summit (D) These immediate reactions are important in demonstrating that the basic response to a sudden increase in aortic resistance consists in development of greater tension with abbreviation of contraction However with each contraction the stroke volume is not quite normal a small amount of blood is retained and with a normal inflow volume quickly increases the presystolic size and initial tension The second stage then supervenes

Curve 10 of figure 26 illustrates the secondary effects in the tenth beat following aortic compression Initial tension is slightly elevated the isometric gradient is steeper the period of isometric contraction decreases and the ejection phase C–F is now prolonged The reactions

of the ventricle to increased initial tension and length obviously become dominant. Changes in the contour of the pressure summits reveal that the pattern of systolic ejection has changed.

Responses of a similar nature follow generalized augmentation of arteriolar resistance such as can be induced by stimulating the cen

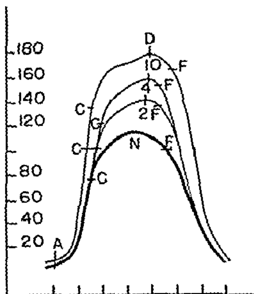


Fig. 26.—Assemblage of transcribed curves indicating changes in left ventricular pressure from normal (N) during the second, fourth, and tenth beats after sudden compression of the aorta just above the diaphragm. In beats 2 and 4 note same initial tension, prolongation of isometric contraction (A C), displacement of summit (D) later in systole and earlier termination of systole at F. In beat 10 note additional effects of increasing initial tension at A, such as steeper isometric gradient, higher systolic pressure (D), and prolongation of systole (A F).

tral ends of the vagus nerves. The myocardial responses are complicated, however, by the greater venous return which follows displacement of blood from minute peripheral vessels and the spleen and by augmentation of coronary flow. Consequently the output of the right heart quickly increases and larger volumes of blood are delivered to the left heart.[4] The rise of initial pressure and the left ventricular

responses are thus accentuated to such an extent that the stroke volume actually exceeds the normal

Aortic Coarctation

Clinical types of aortic coarctation can be simulated by stepwise constriction of the aorta proximal to the left subclavian artery Recent studies by Gupta and myself[1] have shown that the lumen of the aorta must be reduced by 55 to 60 per cent before an elevation

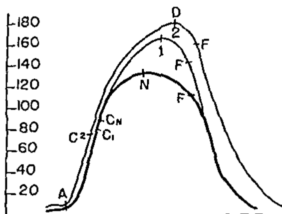


FIG ?—Assemblage of transcribed records showing deviations from a normal left ventricular pressure curve (N) following reduction in aortic lumen just peripheral to subclavian artery by 60 per cent in curve 1 and by 87 per cent in curve 2 Note abbreviation of the isometric phase (A C) the delayed summit (D) and the abbreviation of contraction (A F) curve 1 Also observe the higher initial tension (A) the higher rounded summit (D) and lengthening of systole (A F) in curve 2

of aortic and left ventricular pressures ensues Figure 27 shows some consequences of effective degrees of coarctation Comparison of the curves with those of figure 26 reveals many similarities but there are two important differences In the former aortic diastolic pressure rises in the latter it declines Consequently in coarctation isometric contraction is terminated earlier as indicated at C_1 and C_2 on curves of figure 27 Also initial tension (A) fails to increase until the aorta has been constricted to 80 per cent of its natural diameter As soon as initial tension increases systolic ventricular pressure is elevated still

more as shown in curve 2 of figure 27 and the systolic discharge also *becomes greater*

Since augmented stroke volumes are realized despite a marked reduction in aortic pressure below the coarctation and hence a drastic *decrease in inferior caval flow the inference follows that total venous* return is rebalanced through corresponding augmentation in superior caval and coronary flows The correctness of this deduction had been previously demonstrated in similar experiments performed *in conjunction* with Katz [20] which indicated that right atrial and ventricular pressures may even elevate slightly owing to a somewhat greater total venous return

It has been emphasized that the augmented pulse pressure central to a coarctation is associated with a decline of diastolic pressure Such hemodynamic effects cannot be attributed to an increase in aortic resistance at the site of narrowing or to an augmented stroke volume It became obvious to us however that when an effective constriction exists the capacity of the aortic compression chamber becomes very small and its volume elasticity coefficient *(dP dV)* is greatly increased Now it can be demonstrated on artificial circulation models** [3] that when equivalent stroke volumes need to be taken up in a compression chamber which is less distensible (increase in *dP dV*) the mean pressure alters very little but systolic pressure rises and diastolic pressure falls* Hence Gupta and Wiggers [1] concluded *that the central effects of aortic coarctation are not wholly* due to increased resistance at the locus of coarctation but that they also involve reduction in capacity and distensibility of the compression *chamber The latter is wholly responsible for the reduction of diastolic* pressure and contributes to the elevation of systolic pressure in the aorta and left ventricle

Aortic Stenosis

This pathologic condition is usually studied experimentally by tightening a cord around the aorta in close proximity to the aortic orifice Such a stenosis differs physically from that presented by coarctation in that the aortic compression chamber is entirely abolished and circulatory channels proximal to the stenosis return less blood to the right heart All investigators agree that as in the case of aortic coarctation the aortic orifice must be narrowed to between 60 and

* See figure 7D page 15

70 per cent of its original diameter before *cardiac output per beat* or per minute is reduced (For bibliography see reference 24) Nevertheless narrowing of 15 to 30 per cent suffices to create audible and recordable mumurs

The changes in left ventricular contraction depend on the degree of aortic narrowing In mild degrees of stenosis exemplified by curve

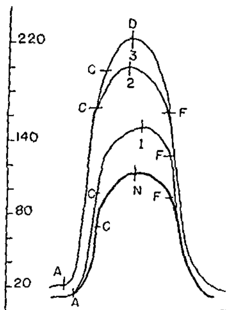


FIG 28 —Transcribed left ventricular pressure curves showing effects of different degrees of aortic stenosis N normal curve 1 = 20 per cent constriction curve 2 = 45 per cent constriction curve 3 = 85 per cent constriction Lettering as in previous figures Description in text

1 of figure 28 the ventricular pressure curves resemble those produced by moderate augmentation of aortic resistance shown in figure 26 initial tension and the isometric pressure gradient remain unaltered but the pressure summit is higher and displaced to a later moment of systole Isometric contraction (A–C) is prolonged slightly but the duration of total systole (A–D) is not affected De Heer[25] who recorded similar curves believed that such reactions typify the effects of aortic stenosis augmentation of aortic resistance was considered

to be the chief determinant of myocardial response. However, Katz and his associates[5] found that the ventricular pressure curves are more peaked as soon as the degree of stenosis becomes dynamically significant. The pressure summit is reached earlier, not later, in systole. Such contraction patterns are shown in the transcribed curves 2 and 3 of figure 27. When ventricular ejection is seriously impeded, the ventricles approach an isometric type of contraction in which the increased residual volume and marked elevation of initial tension contribute to the production of very high systolic ventricular pressure.

It should be kept in mind that the reactions of the left ventricle may be more favorable in experimental than in clinical stenosis. In the former the constriction is peripheral to the coronary orifices, and coronary blood flow is decidedly enhanced; in the latter, the narrowing is proximal to the coronary ostia, and coronary flow is unquestionably reduced. In order to determine whether superposition of coronary insufficiency alters the mechanism of ventricular response, the effects of severe pulmonary stenosis may be analyzed.

Pulmonary Stenosis

Figure 29 contains six segments of records obtained by Fineberg and myself[7] during progressive circular compression of the pulmonary artery. Segments *1* to *3* show steady increases in initial tension, higher systolic summits, and contours similar to those observed in progressive aortic stenosis. It may be noted that the aortic pressures first begin to be affected in segment *3*, in which a 52 per cent reduction in the lumen of the pulmonary artery had been produced. A slightly greater constriction initiates a greater decline of arterial pressure, as shown by segments *4*, *5* and *6* which respectively represent constrictions of [illegible], 59 and 63 per cent of the lumen. The right ventricular pressure curves all display contours typical of an isometric mode of contraction. However, as shown in segments *5* and *6*, the systolic summit rapidly falls with increasing stenosis instead of rising further, as in aortic stenosis (fig. 28). Since such decline of pressure is associated with marked elevation of initial tension, it is a logical inference that myocardial depression due to inadequate coronary flow has supervened.

Summarizing, the ability of the right or left ventricle to overcome the resistance of a narrowed aortic orifice depends as much upon the

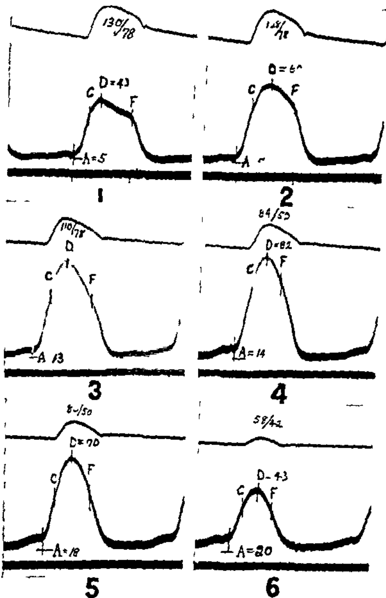


FIG 29 —Segments of records showing changes in aortic pressure (upper) and right ventricular pressures (lower) following stepwise increases of pulmonary stenosis 1 control 2 = 29 per cent constriction 3 = 52 per cent constriction 4 = 56 per cent constriction 5 = 59 per cent constriction 6 = 63 per cent constriction Discussion in text

ability of the myocardium to compensate as upon the actual degree of narrowing The responsiveness of the myocardium in turn depend on the adequacy or insufficiency of coronary blood flow

The abnormalities of ventricular contraction so far considered illustrate conditions in which primary and secondary factors separately or together determine the nature of ventricular responses We turn now to consideration of a few conditions in which tertiary factors play important roles

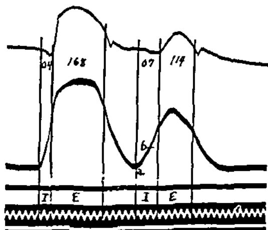


Fig 30 — Aortic (upper) and left ventricular (lower) curves depicting changes during an effective premature contraction *I* isometric phase *E* ejection phase Time 02 second Discussion in text

Idioventricular Rhythms

It is well established that premature ventricular contractions or a succession of such beats during ventricular tachycardia are characterized by delivery of smaller stroke volumes The contraction patterns of a normal and a premature ventricular systole can be compared in the ventricular pressure curves shown in figure 30 The premature beat differs from the preceding normal one in several ways namely the lower systolic pressure summit the changes in contour the prolongation of isometric contraction (I) and an abbreviation of the ejection period (E) sufficient to shorten systole as a whole (I + F) The reduced force and duration of contraction are related to the shorter period of filling in the antecedent beat and consequently a

reduction in presystolic size and initial length Attention may be directed to the fact that the premature contraction starts at a higher initial tension because it begins before relaxation of the previous

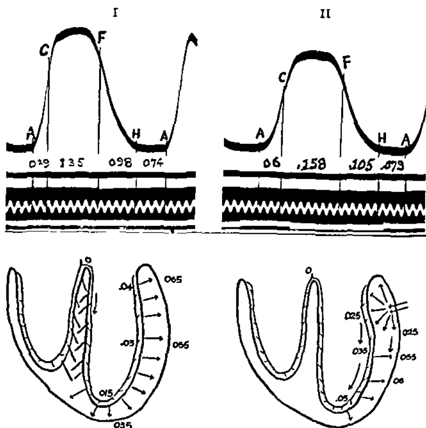


Fig 31 —Comparison of left ventricular pressure curves of same cycle length when excited over normal pathways (*I*) and from a ventricular focus (*II*) The diagrams below compare the approximate order time and direction of the excitation process during excitation from a supraventricular (*I*) and ventricular focus (*II*) Lettering as before Note prolongation of isometric contraction (A C) and ejection (C F) in *II* Time 02 second Discussion in text

beat has been completed This is another illustration of a condition in which initial tension and length change in opposite directions and as previously explained the reactions seem to follow changes in initial

length not those in initial tension However the shorter initial length is not the dominant factor which determines the impairment of ventricular contraction

The basic factor concerned was discovered in 1922[7] by comparing beats of the same cycle length excited from supraventricular and ventricular foci Such records are shown in figure 31 The idioventricular beats (right) arise from the same initial tension as normal beats thereby excluding secondary reactions to initial length Nevertheless beats due to direct ventricular stimulation display a longer isometric contraction (A–C) a prolongation of systolic ejection (C–F) and a conspicuously lower systolic summit These changes are due to the abnormal order and spread of ventricular excitation from an idioventricular pacemaker The concept developed is illustrated by the aid of the diagrams beneath the pressure curves of figure 31 During normal excitation (I) impulses are conducted with great speed to all fractions of the myocardium hence a rapid summation of fractionate contractions takes place When impulses arise from a ventricular focus (II) they spread more slowly at first and in a random fashion with the result that the phasic entry of contractions is delayed As analyzed elsewhere[7] this results in prolongation of contraction and development of less maximal tension In addition the order and direction of spread of the ventricular excitation process determines the mechanical efficiency of contraction During normal excitation over bundle branches the interventricular septum is primarily excited and contracts first A rigid fixation is thus provided around which the ventricular muscle scrolls can contract and empty the ventricles efficiently When excitation arises from the ventricular focus impulses eventually reach the bundle branches but they travel in a reverse direction the septum is excited last and from apex to base The resulting contraction of the ventricle as a whole would appear to be less efficient and may contribute to the lower pressure developed during systolic ejection

To summarize idioventricular beats are less efficient than normal ones because the ventricular pattern of contraction is affected by two factors (a) the abnormal sequence in which fractionate contractions develop and (b) the changes in ventricular filling which occur when the diastole of a preceding beat is abridged The former retards the rate of pressure development and prolongs contraction but re

duces the maximal pressure developed The latter contributes to the slow development of tension and lower systolic pressure through changes in initial length but reduces the period of contraction to such an extent that the lengthening effect due to aberrant excitation is overbalanced hence the ejection phase shortens

Ventricular Alternation

It appears to be the consensus that ventricular alternation is a primary disorder involving abnormal excitation and or contraction of myocardial fractions In 1914 Wenckebach [8] advanced cogent a priori reasons for the concept that some types of alternation may be

Fig 32 —Transcribed curves of left ventricular pressure I control curve before alternation II larger beat and III smaller beat of an alternating couple Lettering as before I_1 I_2 and I_3 indicate the effect that different levels of atrial pressure may have on the time when ventricular inflow begins

induced and sustained by hemodynamic mechanisms which cause alterations of ventricular filling in alternate beats The question therefore arose whether there are two types of ventricular alternation myogenic and dynamic and if so whether means exist for their differentiation One of the first questions that interested the writer [9] in the study of alternation was whether the large as well as the small beat of an alternans couple is abnormal When records were fortuitously obtained at the moment when alternation started spontaneously the surprising discovery was made that the larger beat of an alternans couple is never smaller than the preceding normal one and frequently is even larger (fig 32 curves I II) In such supernormal beats the gradient of isometric contraction is a trifle steeper and

systolic ejection and total systole are both a trifle longer than in preceding normal beats It would appear that the large alternans beat involves no fewer contracting fractions than a preceding normal one Several explanations for such supernormal beats are possible (1) A state of potential alternation may have existed in the beats regarded as normal that is to say an equal number of contracting fractions may be deleted in every beat (2) The increased amplitude and duration may be secondary to a slight increase in presystolic size and initial tension which for some reason accompanies the onset of alternation (fig 32 curve II)

The dynamic differences between large and small beats of an alternans couple are illustrated by curves II and III of figure 32 The smaller beat starts from a slightly lower presystolic pressure it displays a more gradual isometric gradient a longer isometric phase (a–c) a shorter systolic ejection phase (c–d) and a shorter period of total systole (a–d) These changes were attributed by Kahn[3] to deletion of contracting fractions Since pressure also degrades more slowly during isometric relaxation (d–e) Straub[8] laid greater stress on differences in relaxation concluding that alternans develops only when the heart rate is so fast or the contour of the pressure curves so broad that the pressure does not have sufficient time to decline before the next ventricular excitation supervenes



FIG 33 —Aortic (upper) and left ventricular (lower) pressure curves showing the development of temporary alternation (1 2 3 4) after a compensatory pause (C) following a premature contraction (P) N is normal beat Time 04 second

During an investigation of premature ventricular systole the observation was made that a temporary alternation often follows a long diastolic pause[27, 28] A typical response is shown in figure 33 A premature systole (P) succeeds a normal contraction (N) The long compensatory pause (C) allows greater filling of the ventricles and elevates initial tension slightly This could account for the larger

and prolonged post compensatory beat However it is not at once *obvious why beat 2 is so much smaller and why alternation persisted* in beats 3 and 4 and in two more beats not included in the record Further studies revealed that similar reactions follow brief vagal

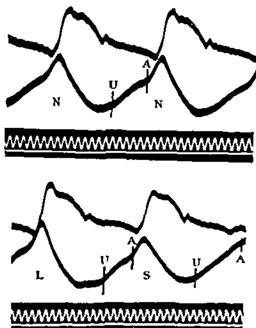


FIG 34 —Two sets of aortic pressure pulses and ventricular volume curves systolic emptying indicated by downstroke in the latter Upper set normal beats lower set changes in larger beat (*L*) and smaller beat (*S*) after development of alternation The stroke volume of smaller beat (S) is less complete and is followed by more gradual filling (U A) The stroke volume of the larger beat exceeds that of normal ones shown in the upper set Discussion in text Time 0 02 second (After C J Wiggers Pressure Pulses in the Cardiovascular System courtesy of Longmans Green London)

stimulation or a temporary A-V block Volume curves of the ventricles such as are reproduced in figure 34 demonstrate that the rate of diastolic inflow is slower in the smaller beat but since the ventricular *expulsion is less complete* the presystolic volume and initial length preceding the larger beat are greater[31] On the basis of such

results it was obvious that alternation can arise during the period of readjustment from a momentary increase in diastolic size. It was emphasized, however, that such alternation is temporary and takes place only when the heart beats rapidly. It is therefore possible that a tendency to alternation exists previous to the disturbance of ventricular filling.

Summarizing my current views, it appears highly probable that ventricular alternation always involves the defection of some fractionate contractions during the smaller beat. However, changes in the intensity of alternation do not necessarily signify quantal variations in the deletion of fractionate contractions. They can be induced by secondary dynamic factors which alter diastolic distention and initial tension. For example, if the residual volume of blood is suddenly increased during a smaller contraction, the addition of a normal inflow volume during succeeding relaxation leads to a larger presystolic volume and initial tension with the result that the amplitude of the larger contraction is augmented. It is for such dynamic reason that a casual irregularity may intensify an existing alternation.

While ventricular alternation usually involves deletion of fractions distributed throughout the myocardium, it may be caused by alternate changes of contraction in only one region. The fact that periodic interruption of blood flow in a coronary ramus frequently results in alternation of the ventricle as a whole afforded Green[34] an opportunity to study the dynamics of alternation accompanying coronary insufficiency. Myographic records from the region of impaired blood supply revealed that three types of alternation may occur. (1) The region may shorten less during the smaller than during the larger beat. (2) It may shorten during the larger and actually stretch during the smaller beat, indicating alternate absence of contractions. (3) It may expand in both the small and the large beats but to a lesser extent in the latter. Green[34] also found that the surface fibers in an ischemic area are stretched to a greater extent before inception of the smaller beats than previous to the onset of the larger ones. He interpreted this as proving that alternation following coronary insufficiency is due to periodic deletion of contractile units and not to alternate responses to changes in initial length. Further support for the localized source of alternating beats in myocardial ischemia was recently offered by the

observations of Hellerstein and Liebow [35] They reported that the S T segment and T wave more rarely the QRS complex alter in epicardial leads *from regions overlying the involved area*

These discussions of alternation following coronary insufficiency offer a natural transition to our next topic

Coronary Occlusion—Myocardial Ischemia

The immediate dynamic effects following experimental coronary occlusion were first analyzed by Orias[36] and have recently been confirmed by Kupfer [37] Representative immediate effects are shown in

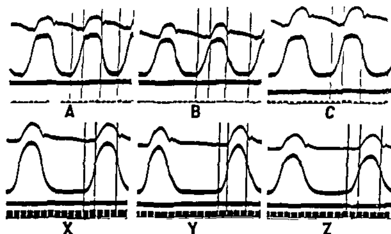


FIG 35 —Aortic (upper) and left ventricular (lower) pressure curves showing *the immediate and delayed effects following occlusion of the ramus descendens anterior* *A* control *B* one minute after coronary occlusion *C* compensation four minutes after occlusion X control from another experiment Y effect two minutes after coronary occlusion *Z* decompensation 15 minutes after occlusion Discussion in text

segment *B* figure 35 *A* and *B* Within a minute after interruption of coronary flow aortic pressures and pulse pressure are reduced and the form of the aortic pressure pulse is altered two phenomena that definitely indicate immediate reduction in systolic discharge The left ventricular pressure curves furnish the explanation for such ventricular impairment The isometric pressure rise is slower but since the semilunar valves open at a lower pre ure this phase may not be

prolonged The period of systolic ejection is abbreviated considerably and the pressure summit is lower and more rounded Orias [16] applying basic information gained from previous studies [4] inferred that these immediate changes are caused by a deletion or impairment of contractions in the block of myocardium within the territory of the occluded vessel In 1935 Tennant and Wiggers[5] demonstrated objec

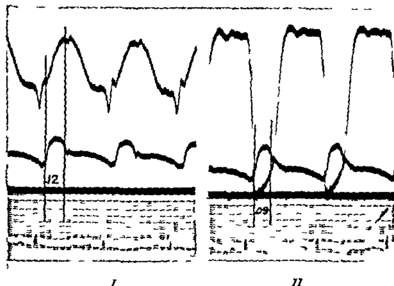


FIG 30 —Two records of myograms from the anterior surface of the left ventricle (upper curve) with aortic pressure pulses and an electrocardiogram (lead II) I a normal control II records obtained two minutes after occluding the ramus descendens anterior Note that in I shortening of the area is indicated by an upward deviation of the curve while in II marked expansion is demonstrated by a downward movement between the two vertical line

tively by myographic tracings that this interpretation is correct As shown in figure 30II approximately within a minute after coronary occlusion the ischemic area no longer shortens but expands brusquely during isometric contraction and either remains so during the remainder of systole or undergoes a slight shortening Given such a hint through experimental observations a number of investigators [18-] have subsequently shown by means of fluoroscopic roentgeno-

graphic and electrokymographic technics that the infarcted area in human cases expands in a similar fashion. Such defective contraction in the potentially infarcted area reduces the total myocardial force for raising intraventricular pressure. In addition, some of the pressure created by still viable portions of the myocardium is spent in stretching the ischemic area and is thus unavailable for expelling blood into *the aorta*.

As shown in segment C of figure 35, taken four minutes after coronary occlusion, the heart has compensatory mechanisms by means of which dynamic conditions can be quickly restored to normal, provided *the remaining myocardium is in good condition. While this* interpretation accords with the general clinical opinion, the experiments just quoted are, to my knowledge, the only ones on record which really demonstrated that compensation occurs not through improvement of collateral circulation in the affected area[43] but through enhanced action of the uninvolved myocardium. Experiments such as these also elucidate the mechanisms by which the rest of the muscle *responds promptly and compensates through increase in diastolic* size and elevation of initial tension.[44] Briefly, the following chain of events takes place. During hypodynamic beats, such as are exhibited in segment B, the ventricle expels less blood; the accumulating systolic remainders added to oncoming blood progressively increase the presystolic volume and pressure in the left ventricle and stretch the viable muscle; this muscle, in accordance with the law of initial tension and length, contracts more vigorously, thereby restoring cardiac output and arterial pressures to normal. Such compensation is illustrated in segment C.

If, on the contrary, the viable ventricular muscle is not in good *responsive condition, progressive deterioration supervenes.* Segments X, Y and Z of figure 35, taken from another experiment, illustrate this type of response. The ventricular pressure summit lowers steadily, systole is shortened and arterial pulse pressures fall progressively despite the fact that initial tension rises steadily. As far as my experimental evidence goes, the circulatory failure which follows is entirely due to myocardial decompensation; there has never been evidence in our studies which indicates that peripheral factors are involved in the circulatory failure.[37, 44] *Circulatory imbalance may, however, supervene* through the development of cardiac irregularities. For instance, repeated premature contractions or atrial fibrillation displace blood

from the arterial to the venous side and to the pulmonary vessels with the result that a *significant hypotension may develop which* is often confused with a true state of shock

The Importance of Cardiac Valves

Yandell Henderson[4] pointed out that the A V and semilunar valves cause the ventricles to contract and relax in a manner similar to that of a skeletal muscle attached to an instrument devised by

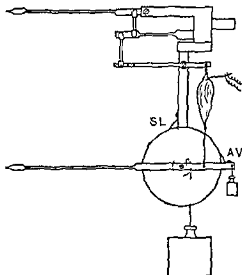


Fig 37 – Diagram illustrating the principle of Fick's work adder Description in text (After Y Henderson courtesy Am J Physiol)

Fick and known as a work adder As illustrated in figure 37 the upper end of a muscle is attached to a stiff spring which can be arranged to record the muscular tension before and during contraction The lower end of the muscle is attached to a movable lever on which a small weight is hung This weight *which corresponds to the input load of* the ventricles lengthens the muscle slightly and creates a small tension previous to contraction (initial length and tension) A ratchet AV upon the toothed wheel of the work adder comparable to the A-V valves *prevents the lever from* moving until sufficient tension has

been developed to overcome the force of a larger weight attached to the toothed wheel This weight which corresponds to the output load of the ventricle is supported during the phases of isometric contraction and relaxation by a second ratchet SL which corresponds to the semilunar valves Such an arrangement causes the muscle to contract in an *after loaded* manner

If we release the ratchet SL the large load acts upon the muscle before contraction starts and a *loaded* type of contraction results A similar situation might be expected when the aortic valves are grossly incompetent If we release the ratchet AV no connection exists with the large wheel to which the heavier weight is attached hence contraction of the muscle would merely raise and lower the small weight and never move the large one A similar situation might be postulated during gross mitral incompetency namely that blood would merely be moved back and forth between the left atrium and ventricle without any discharge into the aorta Obviously neither of these postulated effects actually takes place in the heart which can still propel blood after deletion of all valves The physical and physiologic reactions which make this possible need to be considered

Aortic Regurgitation

The dynamics of this valvular lesion which has interested me since 1915 involves three problems (1) the mechanisms by which systolic discharge is essentially restored to normal (2) the time of regurgitation during diastole and (3) the factors which determine the regurgitated volume (For bibliography see references 24 46 47)

The immediate effect of an aortic leak is a reduction in the net stroke volume a smaller aortic pulse pressure and an increase in the diastolic ventricular volume When the myocardium is in good condition it responds at once to the greater initial length and tension with a more vigorous contraction As a result the tidal volume expelled from the ventricle increases considerably The loss of pressure which occurs during diastole results in a very low end diastolic pressure in the aorta Since systolic pressure is generally elevated through the augmented systolic discharge the aortic pulse pressure is extremely large These changes are illustrated in figures 38 and 39

Wiggers and Maltby[48] discovered that the reaction patterns of the left ventricle depend to a considerable extent on the size of the aper

ture The effects produced by small leaks are shown in figure 38 The initial tension is increased at A and the isometric contraction phase (A–C) is shorter because expulsion of blood starts at a lower aortic pressure (C) The increased durations of ejection (C–F) and of total systole (A–F) are reactions to the higher initial tension The

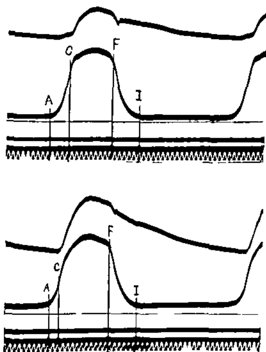


FIG 38 —Upper records normal aortic and left ventricular pressure pulses Lower records same after production of a comparatively small aortic valvular leak A C isometric contraction C–F ejection phases F I relaxation to basic pressure levels

summit of the pressure curve is reached earlier because the ventricle *empties itself more completely during the early portion of ejection* when aortic pressure is still abnormal Summarizing the pattern of ventricular contraction as exhibited by the form of left ventricular pressure curves is a resultant of (1) the lowered aortic resistance during the early part of contraction and (2) the compensatory effect

produced by a greater presystolic stretch and elevation of initial tension

When the aortic leaflets are spread wide apart so as to allow maximum reflux during diastole the pattern of ventricular contraction is further changed because the full aortic load plays on the left ven

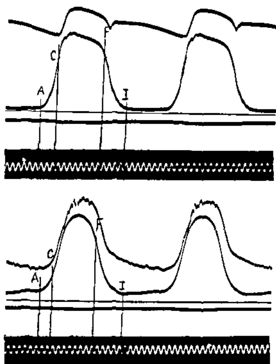


Fig 39 —Upper records normal aortic and left ventricular pressure pulses Lower records same after production of a maximum *aortic valvular insufficiency* Lettering as in figure 38

tricle and it contracts in a loaded manner Such contractions tend to be of shorter duration than isometric types of contraction The effects on left ventricular pressure curves are illustrated in figure 39 The elevation of initial tension is unquestionably responsible *for the de*velopment of a higher systolic pressure and the ejection of larger tidal volumes into the aorta The latter can be inferred directly from

the large aortic pulse pressure which starts from a lower diastolic pressure However, in the majority of cases the expected lengthening of total systole is neutralized by the loaded manner of contraction

It might be expected that an isometric contraction period could not exist in a loaded contraction Actually records that are reproduced in figure 39 indicate that a brief rise of ventricular pressure (A–C) still occurs before aortic pressure starts to rise This delay is explained by the facts that the current of blood in the ventricle must be reversed and that aortic diastolic pressure slightly exceeds that in the ventricles

The records of figures 38 and 39 show clearly that the time of diastolic regurgitation depends on the size of the aortic orifice With openings of small and moderate size (fig 38) the gradient and duration of isometric relaxation remains unaltered the chief decline of aortic pressure occurring after completion of isometric relaxation at I Hence the inference that significant regurgitation does not take place until relaxation has progressed to a pressure level at which the mitral valves open In this way a dynamic situation is created in which flow from the left atrium competes for ventricular space with that through a leaking aortic valve (See also fig 10 Chapter I)

On the contrary when the semilunar valves are widely separated aortic pressure falls abruptly to a low level during the time the left ventricle relaxes (fig 39 F–I) and consequently declines comparatively little during the remainder of diastole The inference follows logically that in very large leaks regurgitation takes place immediately during the decrease of ventricular tension It may be added parenthetically that this period corresponds to isometric relaxation in the normal heart but cannot be designated as such since the ventricle contracts as a loaded not as an afterloaded muscle The slow elevation of tension after I in figure 39 is attributable to ventricular filling from the left atrium

The influence that the size of the leaking aortic orifice has on the regurgitant volume has been studied from physical and engineering standpoints on models as well as on dead hearts (For bibliography see references 24 46 47) Experimental work convinces us however that the magnitude of regurgitation depends as much on the successive pressure differences as on the size of the leaking orifice As a matter of fact for purely physical reasons the total pressure difference di

minishes as the size of the leaking orifice increases The hydraulic principles can be gleaned from the illustration in figure 40 in which aortic pressure curves simulating those obtained after large and small leaks are superimposed on a common ventricular pressure curve The successive diastolic gradients in the case of smaller leaks are represented by the area C_Y and those in the case of larger leaks by the area $C_X + C_Y$

In former years I defended the view previously suggested by Stewart that the percentage of the tidal volume which regurgitates remains relatively small even when valves are grossly deficient Subsequent observations in our own[46, 47] and other[48] laboratories demon

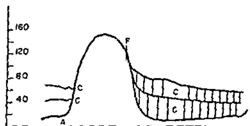


FIG 40—Diagram showing that the diastolic pressure differential between aorta and left ventricle is less in the case of small sized aortic orifices (C_Y) than in large ones ($C_X + C_Y$)

strated however that regurgitation volume may increase up to 60 per cent of the tidal volume with large aortic openings

Mitral Insufficiency

It is generally conceded on the basis of animal experiments that the reduction in systolic discharge which results from reflux of blood into the left atrium is somehow compensated by mobilization of a larger tidal volume In 1922 Wiggers and Feil[49] elucidated the compensatory mechanisms concerned through registration of pressure pulses from the left atrium and ventricle Our studies indicated that the sudden creation of a mitral leak is succeeded by the following train of events By virtue of the systolic backflow through incompetent valves the volume of blood discharged into the aorta during each systole is reduced As illustrated in figure 41 maximal ventricular tension is lowered immediately, but it increases gradually as initial

pressure rises At the same time the pressure in the left atrium increases and the curves show a marked systolic elevation with murmur vibrations superimposed Under the greater head of pressure at F the left ventricle fills more completely and the effects of augmented initial tension and presystolic volume come into play Maximal intraventricular pressure increases steadily and the duration of systole is slightly prolonged

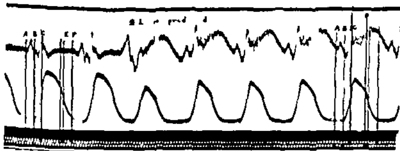


FIG 41—Pressure curves in left atrium (upper) and left ventricle (lower) illustrating immediate and stabilized effect of rendering the mitral valves suddenly insufficient A B atrial systole B-C, isometric ventricular contraction C D ejection phase E F isometric relaxation Time 0? second Note superposition of systolic murmur vibrations on atrial curve Description in text (After Wiggers and Feil courtesy of Shaw and Sons London.)

The records of figure 41 show other interesting details Comparisons of phasic pressure changes in the left atrium and ventricle demonstrate that even when a static equilibrium has been reached left atrial pressure rises only to a minimal extent during isometric contraction indicating that no significant regurgitation takes place during this phase The main elevation of left atrial pressure and the real regurgitation occur simultaneously with discharge of blood into the aorta Furthermore regurgitation does not terminate precisely with systole for atrial pressure continues to rise at a reduced rate during the period of isometric relaxation These times of regurgitation are corroborated by registration of volume changes of the left atrium by special forms of cardiometers Such records are shown in figure 42 When regurgitation exists the left atrial volume decreases during atrial systole (A–B) increases very little during isometric ventricular

contraction (B–C) augments rapidly and considerably during the *period of systolic ejection (C–D), and continues to increase for 0 08* second during isometric relaxation of the ventricle (D–E) During the succeeding rapid inflow phase (F–T) the volume of the left atrium decreases rapidly as it empties into the left ventricle

Physical factors alone account for such a time course of regurgitation Since the isometric contraction phase is very short (0 04 to 0 05 second) and the pressure increases roughly from 4 to 70 mm Hg the inertia of blood within the ventricle cannot be quickly overcome and the blood is not set in backward motion until the aortic valves have opened Thus any considerable reflux is dynamically impossible even *when openings of considerable size exist On the contrary systolic* ejection lasts from 0 15 to 0 25 second and the intraventricular pressure ranges from 70 to 160 mm Hg The continuance of such pressures over a longer time interval determines the considerable backflow during systolic ejection Finally since ventricular pressure still exceeds intra atrial during isometric relaxation equal to 0 08 to 0 09 second regurgitation continues despite the fact that diastole is actually in progress

That these types of regurgitation do not involve mechanisms peculiar to the heart but are determined by physical factors can be *demonstrated successfully by simple apparatus illustrated in figure* 43 The device consists of a chamber (A) to which an optical manometer (M) recording the pressure within it is attached The pressure is increased by rapid compression of a large bulb (B) Fluid is thus displaced either through a valveless tube into a bottle (C) against a fluid column varying from 60 to 150 mm H_2O or by a larger tube through a valve into a second receptacle (F) containing a mercury column equal to 60 or 80 mm Hg Time relations of regurgitation to pressure development, as well as the volume actually regurgitated into the bottle (O) under different pressure conditions may be optically recorded by connecting the bottle (C) to a tambour (D) attached to an optical capsule (T)

Figure 44 shows a record in which the pressure variations in the system simulate those in the heart As pressure rises rapidly to a point corresponding approximately to the isometric phase (A–B) the regurgitation indicated by the darker curve is exceedingly light During the subsequent rise and fall of pressure (B–C) corresponding

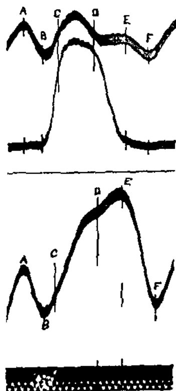


Fig. 42.—Volume changes of the left atrium related to a left ventricular pressure curve. Upper volume curves during normal action of A-V valves. Lower volume curves adjusted to same ventricular pressure curve but taken after production of mitral insufficiency. A-B, decrease in atrial volume during atrial systole. B-C, slight increase in volume during isometric contraction in both curves. C-D, more marked increase in volume during systolic ejection in lower curve. D-E, continued volume increase during isometric relaxation in lower curve. E-F, more marked reduction in atrial volume during rapid inflow phase in lower curve. (After Wiggers and Feil, courtesy Shaw and Sons, London.)

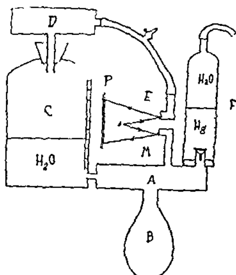


FIG 43 —Physical model to demonstrate regurgitation and forward movement or a liquid Description in text (After Wiggers and Feil [49] courtesy Shaw and Sons London)

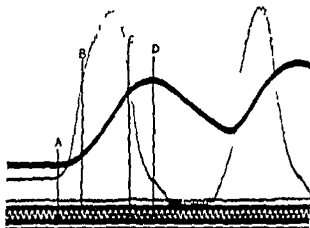


FIG 44 —Records of pressure (lighter curve) and periods of regurgitation obtained when bulb of apparatus shown in figure 43 is compressed to simulate ventricular pressure changes A B isometric rise of pressure B C period of output into mercury chamber C D relaxation of bulb Description in text (After Wiggers and Feil [49] courtesy of Shaw and Sons London)

roughly to the ejection phase a larger volume is regurgitated As in the heart this backflow does not cease when compression is stopped at C but continues until D It can also be demonstrated that such a physical phenomenon is conditioned upon a rapid compression of the bulb If the bulb is squeezed very slowly and the pressure elevated very gradually backflow starts at once and regurgitation becomes large during the isometric period which is thereby also prolonged The bulb may indeed be compressed so slowly that its entire contents are emptied into the bottle The inference is clear the volume of regurgitation is conditioned not only by the size of the leak and the mean pressure in the ventricle but also by the velocity of tension development during isometric contraction Given the same orifice more blood regurgitates when ventricular contractions become hypodynamic

Herein lies the real compensatory importance of good muscular action during mitral insufficiency Failure of the myocardium to respond adequately to the increase in initial tension results in a series of events which end in decompensation The seriousness of the valvular lesion consists in the fact that the patient or animal with incompetent mitral valves has lost a factor of safety by which slight cardiac depression can be readily withstood Mitral insufficiency is dangerous primarily not by virtue of the circulatory changes induced through valvular deficiency but on account of the constant liability to decompensation from any cause which weakens ventricular contraction Finally attention may be directed to the fact that since the rate of pressure increase is such an important determinant of the volume regurgitated calculation of the size of leaking orifices from laws based on static equations do not necessarily apply to the beating heart

Mitral Stenosis

It has been recognized for centuries on a priori reasoning (Vieussens 1715) that narrowing of the mitral orifice introduces a resistance to the flow of blood from the left atrium into the ventricle thereby impairing its filling and systolic output This was confirmed by careful studies on artificial models and by early experimental work It was generally agreed that marked degrees of mitral narrowing cause a reduction in stroke volume a decline of arterial pressure and a decreased venous return to the right heart The consistent rise of left

atrial pressure causes pulmonary congestion and according to most observers an increase in pulmonary arterial pressure The consensus has been that right atrial and systolic right ventricular pressures fall (For reviews see reference 24)

In 1931 Katz and Siegel[51] properly called attention to the difficulty of producing this lesion experimentally without introducing secondary changes in the circulation Using the purse string suture method however they consistently found an immediate reduction in systolic *left ventricular and aortic pressures with a reduction in aortic pulse* pressure and a pronounced elevation of left atrial pressure The amplitude of the atrial contraction wave increased markedly The effects on pulmonary arterial and right ventricular pressures again proved variable probably depending on the condition of the circulation at the time of observation In some experiments systolic pressure rose in the right ventricle and pulmonary artery pulse pressure increasing in other experiments however it decreased and with it the systolic and pulse pressures in the pulmonary artery fell

In restudying the interrelations of right and left atrial pressure Brecher and Opdyke[5] found that right atrial pressure shows a slight *mean elevation chiefly due to an increase in the atrial contraction* wave for the pressure at the time the tricuspid valve opens was slightly reduced It is improbable therefore that results indicating a decreased force of right ventricular contraction represent standard dynamic consequences of mitral stenosis Current studies by Ankeney[53] reveal that pulmonary capillary pressure also rises but the pulmonary vascular resistance prevents the transmission of phasic pressure change as claimed by some investigators

The dynamic effects of extreme mitral stenosis are of course determined by the size of the mitral orifice for it is obvious that sufficient pressure cannot be developed in the left atrium to overcome the *great resistance to flow through a very small slit or bagging funnel* When the stenosis is not too extreme however the dynamic consequences are governed as much by the effectiveness of compensatory mechanisms as by the size of the mitral orifice Katz and Siegel[5] list three important mechanisms by which a variable improvement in ventricular influx can be brought about (1) the elevation of left atrial pressure during the early diastolic period of ventricular filling (2) the consistent abbreviation of ventricular systole and correspond

ing extension of the diastolic filling period (3) the augmentation of left atrial contraction as a result of its greater diastolic stretch and the consequent development of a high atrial pressure A further suggested mechanism has not stood the test of time When these compensatory mechanisms are abrogated as during tachycardia or atrial fibrillation circulatory decompensation can develop suddenly

In view of the relation of compensatory mechanisms to the size of the mitral orifice a number of attempts have been made to determine the maximum degree of stenosis consistent with approximately normal cardiac output during rest and exercise Hydrodynamic studies by Allan[64] on artificial valves in a physical system led to the conclusion that a reduction of surface area by 75 per cent can take place without marked increase in resistance Simple tests by the writer[21] on excised hearts of recently killed dogs seemed to confirm these findings for the valvular orifice could be occluded by sounds equal to 61 per cent of the orifice without impeding flow from the left atrium under a pressure of only 14 cm H_2O The problem has recently been attacked in a more thorough manner by Gorlin and Gorlin [64] They developed a formula which permits calculation of the size of the mitral orifice by means of information now obtainable from patients viz

$$\text{Mitral area} = \frac{\text{mitral valve flow}}{31\sqrt{\text{pulmonary capillary pressure minus 5 mm Hg}}}$$

Patients with mitral orifices of 2 5 sq cm compensated well Those with orifices of 1 3 to 1 6 sq cm experienced limitation of activity Subjects with valve areas of 0 6 to 1 1 sq cm had very limited activity and those in which reduction to 0 4 to 0 9 sq cm existed were confined to bed or chair

In conclusion it is apparent that experimental work has not as yet satisfactorily established the dynamic reactions of the right ventricle to various grades of mitral stenosis The common observation that initial tension and systolic pressure are reduced in the right ventricle is difficult to square with the frequent development of right ventricular hypertrophy However it should be remembered that clinical forms of severe mitral stenosis also lead to alterations in the pulmonary vascular system the superimposed effects of which have not as yet been reproduced experimentally For these reasons the clinical study

of the dynamics of mitral stenosis continues to remain a fruitful field for further exploration

Summary

Selected types of experiments carried out in our laboratory during the past 33 years relevant to the interpretation of clinical disorders are reviewed From an analysis of ventricular pressure pulses inferences were drawn as to basic determinants of cardiac performance in experimental conditions simulating those which arise clinically The analysis included alterations in ventricular contraction patterns produced by pericardial effusion hypervolemia oligemia arterial hypertension of peripheral origin and that due to coarctation of the aorta aortic and pulmonary stenosis idioventricular rhythms ventricular alternation coronary occlusion and myocardial ischemia aortic regurgitation and mitral insufficiency

1 The following principles were emphasized for guidance in interpreting ventricular pressure curves Investigators who attempt to analyze the mechanisms of cardiac adaptation from ventricular pressure pulses should first satisfy themselves that the recorded curves accurately depict the pressure changes i e that they are not deformed by artefacts or that when present these can be di counted They must be able to translate changing pressure values gradients and inflections presented by ventricular pressure curves into mental pictures of dynamic processes The integration of pressure pulses from the left atria ventricle and aorta with myographic and acoustic phenomena volume changes in the ventricles and electrical phenomena once considered as academic exercise, has become an inescapable requirement in the current era of hemodynamic investigations

2 As Starling has pointed out the responses of the myocardium under many normal and pathologic conditions are determined by changes in the presystolic size of a ventricle that is the initial length of its fibers Per onal experience has confirmed Frank s earlier postulate that under ordinary conditions changes in initial length are p o duced by alterations in ventricular pressure at the on et of contractions, that is the initial tension

3 The law of initial length and tension so formulated assumes the existence of controlled conditions Con equently their determinant effect on force magnitude and duration of contraction can be sat s

factorily studied only when the following conditions obtain (a) the cycle length must remain constant (b) the basic condition of the myocardium must remain the same otherwise its response varies at identical initial tension and length and (c) conditions which change the mode of ventricular contraction in mechanical ways must not be operative

4 Under such controlled conditions changes in the force amplitude and duration of ventricular pressure curves accompanied by an elevation of initial tension can be referred to the beneficial effects of stretch Such a dominant control of the contraction patterns is illustrated by responses to increased and decreased venous return during respective states of hypervolemia and oligemia

5 When the reactivity of the myocardium is enhanced or depressed through local metabolites fatigue humoral agents nervous actions or inadequate coronary flow the ventricular responses alter without changes in initial tension or more commonly with changes in an opposite direction Thus following the use of cardiac depressant drugs *or prolonged hypotension such as occurs in shock the force magni*tude and duration of ventricular contractions decrease through primary myocardial depression and this leads to elevation of initial length and tension

6 Under special conditions initial tension and length may deviate in opposite directions in which case the reactions are determined by changes in initial length This happens during large pericardial effusions for the elevated pericardial pressure is transferred to the ventricular cavity at the same time that diastolic filling is hindered The ventricles develop less pressure and their contraction is abridged despite an elevation of initial tension A similar dissociation of initial tension and length supervenes when a premature ventricular systole starts before the preceding beat has relaxed completely Mechanical impairment of filling also operates to dissociate initial tension and pressure in ventricular tachycardia and alternation but it is not basically important in determining the contraction pattern

7 The slower and smaller contractions displayed by beats of ventricular origin are produced by a slower entry of fractionate contractions combined with failure to fix the septum primarily Similarly the apparent depression of myocardial contraction exhibited by the smaller beat of an alternans couple is caused by deletion of some frac

tionate contractions There is no evidence that the inherent reactivity of muscle fractions participating in contraction is changed There is good evidence that they respond to secondary changes in initial tension and length which may either augment or counteract the effect of aberrant myocardial contractions Depression of ventricular contraction which follows coronary occlusion almost immediately is likewise *due to enfeeblement or absence of contraction in the infarcted* area but complete compensation may result from response of viable muscle to increases in initial tension and length On the other hand myocardial depression may *supervene and intensify the hypodynamic* response of the left ventricle leading to circulatory failure

8 It must be obvious from data so far analyzed that the establishment of concordant or discordant changes in initial tension (or atrial *pressures) and contraction patterns in uncontrolled or abnormal con*ditions cannot be cited to validate or invalidate the operation of the law of initial tension and length

9 A careful study of left ventricular pressure curves has revealed that the law of initial tension and length determines the ventricular responses under grossly abnormal conditions but the resulting contraction patterns are modified more or less through operation of *other coefficients (a) In aortic hypertension due to increased periph*eral resistance the force of contraction is enhanced and its duration tends to be curtailed through action of a greater output load (b) In aortic coarctation the ventricular effects of increased resistance and rise of initial tension are decidedly modified by the fact that the left ventricular contents must be displaced into a smaller and less distensible compression chamber (c) In aortic stenosis the effects of *increased initial length and augmented resistance on ventricular con*traction are modified by the shift from an afterloaded to a more nearly isometric type of contraction (d) In severe aortic insufficiency the increased initial length and tension are responsible for the compensatory increase in force of contraction but their effects on the ventricular contraction pattern are modified through a shift from an afterloaded to a loaded type of contraction (e) Existence of *incompetent mitral valve modifies the ventricular response through changes in initial tension but the ventricular contraction pattern* is modified because a part of the tidal volume regurgitates into the left atrium

(f) While the dynamic effects of mitral stenosis are dominantly determined by the size of the mitral orifice in the case of very severe lesions they are largely a result of the effectiveness or ineffectiveness of compensatory reactions when lesions are not extreme

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